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Supporting Information

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Nickel-Catalyzed Carbon–Nitrogen Bond Formation on the β-Carbon of Saturated Ketones

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Supporting Information

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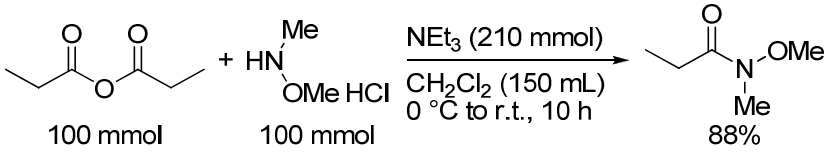
I. General and Materials.

NMR spectra were measured with Bruker AVANCE 400 (9.4 T magnet) spectrometer. In ^{1}H NMR spectra, chemical shifts (ppm) referenced to internal tetramethylsilane (δ 0.00 ppm, in $CDCl_3$). In ^{13}C NMR spectra, chemical shifts (ppm) referenced to the carbon signal of the deuterated solvents (δ 77.0 ppm in $CDCl_3$). ^{1}H NMR data are quoted as chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz), relative intensity. GC-MS analyses were performed on an Agilent Technologies 6890N (G1530N) equipped with a JEOL JMS-Q1000GC/DIP MS and an HP-5 column (30 m length × 0.32 mm i.d. × 0.23 μm film). IR spectra were measured with JASCO FT/IR-4100. Elemental and high resolution (FAB) mass analyses were performed by Service Centre of Elementary Analysis of Organic Compounds and Institute for Materials Chemistry and Engineering (ICME) in Kyushu University, respectively. Flash column chromatographies were performed with silica gel 60 (230-400 mesh, Merck). GC analyses were performed on an Agilent Technologies DB-1 (15 m length × 0.250 mm i.d. × 0.10 μm film). The temperature program of GC analyses was 120 °C for 0.5 min, followed by a ramp from 120–280 °C at 40 °C/min and constant temperature for 3.5 min.

Chlorobenzene, propiophenone (**1a**), piperidine (**2b**), dibutylamine (**2c**), diethylamine (**2d**), and dibenzylamine (**2e**) were purchased from Tokyo Chemical Industry Co., Ltd. $Ni(cod)_2$ was purchased from Strem Chemicals, Inc. A sealed bottle of 1 M THF solution of PMe_3, and $Ni(acac)_2$ were purchased from Aldrich Chemical Co., Inc. and used without any purification. Dioxane and K_3PO_4 were purchased from Wako Pure Chemical Industries, Ltd. Morpholine (**2a**) and $NiCl_2$–$6H_2O$ was purchased from Kishida Chemical Co., Ltd. K_3PO_4, $NiCl_2$–$6H_2O$ and $Ni(acac)_2$ were used after the powders were heated under reduced pressure enough to remove water. $NiCl_2(PMe_3)_2$[1] and $NiCl(Ph)(PMe_3)_2$[2] were prepared according to literature procedures. Aminoketone **8** was prepared according to literature procedures.[3]

II. Preparation of Ethyl Ketones 1.

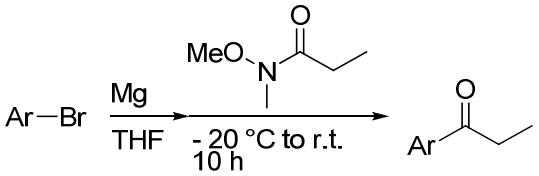
***N*-Methoxy-*N*-methylpropionamide** [CAS No. 104863-65-2].



The Weinreb amide was prepared by slightly modification of a literature procedure.[4] A slurry of *N,O*-dimethylhydroxylamine hydrochloride (9.8 g, MW: 97.54, 100 mmol) in dichloromethane (150 mL) under an N_2 atmosphere was cooled to 0 °C. Triethylamine (29 mL,

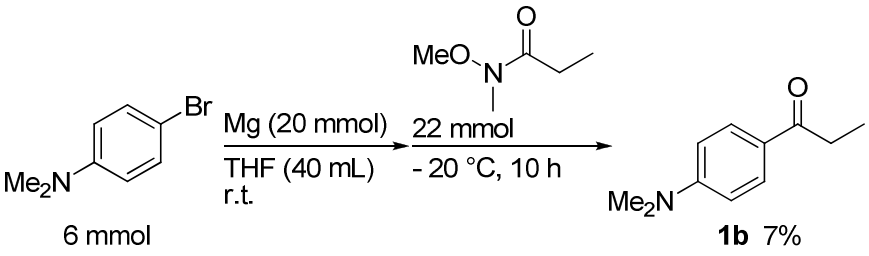
MW: 101.19, *d* 0.726 g/mL, 210 mmol) and propionic anhydride (12.8 mL, MW: 130.14, *d* 1.015 g/mL, 100 mmol) was slowly added. After stirring for 10 h at room temperature, water (100 mL) was added, extracted with EtOAc, dried over $MgSO_4$, and concentrated to provide the Weinreb amide as a clear oil (10.3 g, MW: 117.15, 87.9 mmol, 88%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.14 (t, *J* = 7.4 Hz, 3H), 2.45 (q, *J* = 7.4 Hz, 2H), 3.19 (s, 3H), 3.68 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 8.67, 25.1, 32.2, 61.1, 175.4. This material was used for further reactions without purification anymore.

General Procedure for the Synthesis of Aromatic Ethyl Ketone from Grignard Reagent and Weinreb Amide.



Some ethyl ketones were prepared from Grignard reagents and the Weinreb amide according to the literature procedure.[4] A solution of aryl bromide in THF (1.0 M) was added to magnesium (1.2 equiv.) at room temperature to prepare the Grignard reagent under nitrogen. The Grignard reagent was added to a 1.0 M THF solution of the Weinreb amide (1.5 equiv.) at –20 °C. The reaction mixture was stirred at room temperature for 10 h, and quenched with water. The solution was extracted with EtOAc, dried over $MgSO_4$, filtered, and then evaporated under reduced pressure. After silica gel column chromatography on silica gel (hexane:EtOAc), the ethyl ketone derivative was obtained.

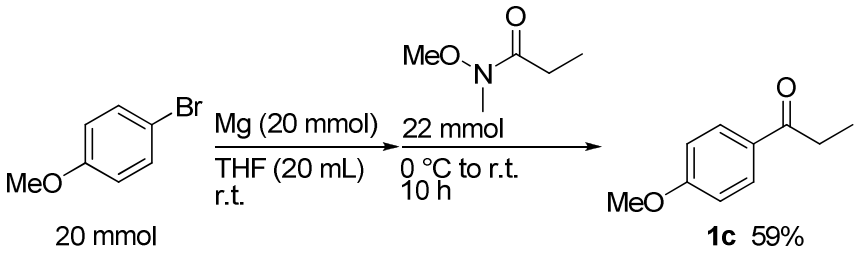
1-(4-(Dimethylamino)phenyl)propan-1-one (1b) [CAS No. 2662-58-2].



The general procedure was followed with use of *N*,*N*-dimethyl-4-bromoaniline (1.2 g, MW: 200.18, 6.0 mmol). The crude product was purified with a silica gel column chromatography (hexane:EtOAc = 10:1 to 5:1) to give **1b** (70.8 mg, MW: 177.24, 7%) as a colorless oil. Spectroscopic data for this compound matched the previously reported literature values.[5] ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.21 (t, *J* = 7.3 Hz, 3H), 2.91 (d, *J* = 7.3 Hz, 2H), 3.05 (s, 6H),

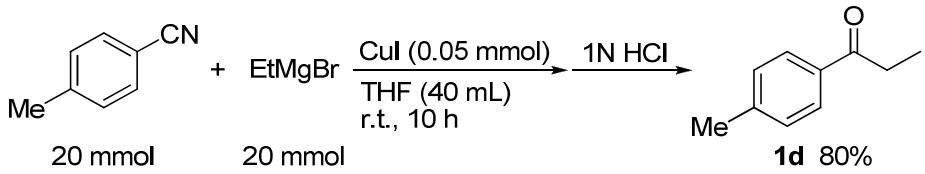
6.66 (d, J = 8.8 Hz, 2H), 7.89 (d, J = 8.8 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 8.83, 31.0, 40.0, 94.7, 110.6, 130.1, 153.3, 199.2.

1-(4-Methoxyphenyl)propan-1-one (**1c**) [CAS No. 121-97-1].



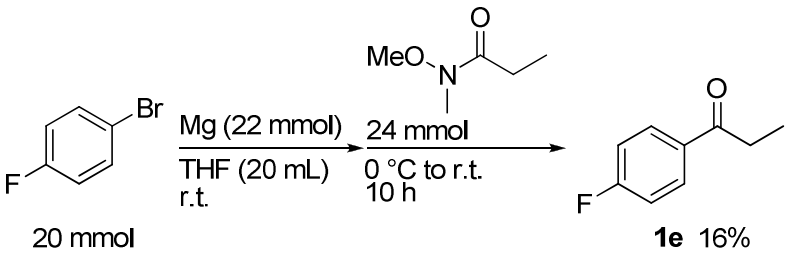
The general procedure was followed with use of 4-bromoanisole (3.7 g, MW: 187.03, 20 mmol). The crude product was purified with a silica gel column chromatography (hexane:EtOAc = 20:1) to give **1c** (1.95 g, MW: 164.20, 59%) as a colorless oil. Spectroscopic data for this compound matched the previously reported literature values.[6] ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.21 (t, J = 7.3 Hz, 3H), 2.95 (q, J = 7.3 Hz, 2H), 3.87 (s, 3H), 6.93 (d, J = 8.8 Hz, 2H), 7.95 (d, J = 8.8 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 8.42, 31.4, 55.4, 113.6, 130.0, 130.2, 163.3, 199.4.

1-*p*-Tolylpropan-1-one (**1d**) [CAS No. 5337-93-9].



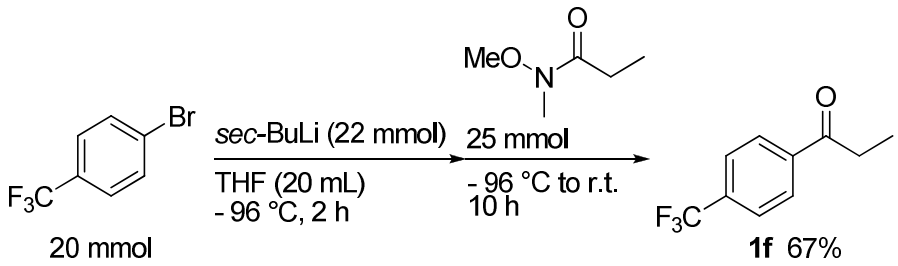
Ethyl magnesium chloride, prepared *in situ* from ethyl bromide (2.2 g, MW: 108.97, 20 mmol) and magnesium (0.49 g, MW: 24.31, 20 mmol) in THF (20 mL), was added to a mixture of 4-methylbenzonitrile (2.34 g, MW: 117.15, 20 mmol) and CuI (10 mg, MW: 190.45, 0.05 mmol) in THF (20 mL) at room temperature for 10 h. After 1 N HCl *aq.* was added at 0 °C, the reaction mixture was stirred at room temperature for 4 h. The organic layer was separated and the remaining aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated. The crude product was purified via silica gel column chromatography (hexane:EtOAc = 10:1) to give a colorless oil (2.37 g, MW: 148.20, 16 mmol, 80%). Spectroscopic data for this compound matched the previously reported literature values.[7] ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.22 (t, J = 7.4 Hz, 3H), 2.41 (s, 3H), 2.98 (q, J = 7.4 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 7.87 (d, J = 8.2 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 8.31, 21.6, 31.6, 128.1, 129.2, 134.4, 143.5, 200.5.

1-(4-Fluorophenyl)propan-1-one (**1e**) [CAS No. 456-03-1].



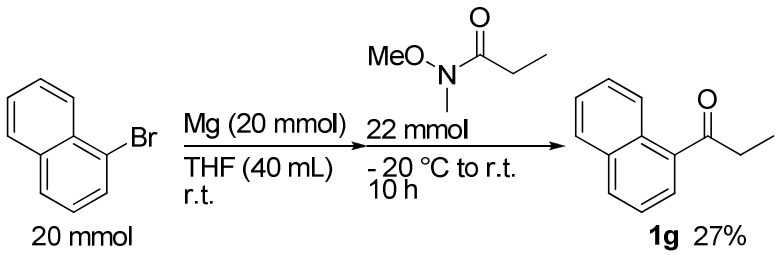
The general procedure was followed with use of 4-fluorobromobenzene (3.5 g, MW: 175.00, 20 mmol). The crude product was purified with a silica gel column chromatography (hexane:EtOAc = 20:1 to 10:1) to give **1e** (0.49 g, MW: 152.17, 3.2 mmol, 16%) as a colorless oil. Spectroscopic data for this compound matched the previously reported literature values.[8] ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.23 (t, J = 7.3 Hz, 3H), 2.98 (q, J = 7.3 Hz, 2H), 7.12 (d, J = 8.6 Hz, 1H), 7.14 (d, J = 8.6 Hz, 1H), 7.83 (d, J = 5.6 Hz, 1H), 8.01 (d, J =5.6 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 8.19, 31.7, 115.6 (d, J = 21.8 Hz), 130.5 (d, J = 9.2 Hz), 133.3 (d, J = 3.0 Hz), 165.6 (d, J = 254.2 Hz), 199.1.

1-(4-(Trifluoromethyl)phenyl)propan-1-one (**1f**) [CAS No. 711-33-1].



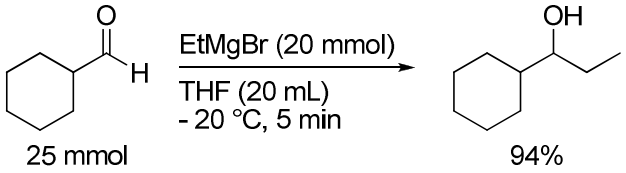
The titled compound was prepared from 4-trifluoromethylphenyllithium reagent, generated from 4-trifluoromethylphenylbromide and *sec*-BuLi, and Weinreb amide. A solution of 1-bromo-4-(trifluoromethyl)benzene (4.5 g, MW: 225.01, 20 mmol) in THF (20 mL) was cooled to – 96 °C. To the solution was slowly added *sec*-BuLi in hexane (22 mmol, 0.96 M, 23 mL), warmed to room temperature and stirred for 10 h. The resulting mixture was quenched with 1 *N*HCl *aq.*, extracted with EtOAc (3 × 50 mL), dried over $MgSO_4$, and concentrated. After silica gel column chromatography (hexane:EtOAc = 20:1), the titled compound **1f** was obtained (2.7g, MW: 202.17, 13.4 mmol, 67%). Spectroscopic data for this compound matched the previously reported literature values.[9] ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.24 (t, J = 7.2 Hz, 3H), 3.03 (q, J = 7.2 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H), 8.06 (d, J = 8.0 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 7.7, 31.9, 123.5 (q, J = 272.5 Hz), 125.4 (q, J = 3.2 Hz), 128.1, 134.0 (q, J = 32.7 Hz), 139.5, 199.4.

1-(Naphthalen-1-yl)propan-1-one (**1g**) [CAS No. 2876-63-3].

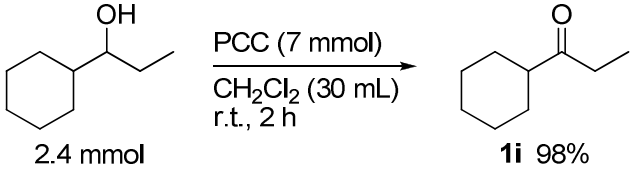


The general procedure was followed with use of 1-bromonaphthalene (4.1 g, MW: 205.07, 20.0 mmol). The crude product was purified with a silica gel column chromatography (hexane:EtOAc = 30:1 to 10:1) to give **1g** (0.97 g, MW: 184.23, 5.3 mmol, 27%) as a colorless oil. Spectroscopic data for this compound matched the previously reported literature values.[10] ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.29 (t, J = 7.4 Hz, 3H), 3.08 (d, J = 7.4 Hz, 2H), 7.47–7.60 (m, 3H), 7.83–7.89 (m, 2H), 7.97 (d, J = 8.0 Hz, 1H), 8.55 (d, J = 8.8 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 8.64, 35.4, 124.3, 125.8, 126.4, 127.1, 127.7, 128.3, 130.1, 132.2, 133.9, 136.2, 205.3.

1-Cyclohexylpropan-1-one (**1h**) [CAS No. 1123-86-0] and **1-Cyclohexylpropan-1-ol** [CAS No. 17264-02-7].



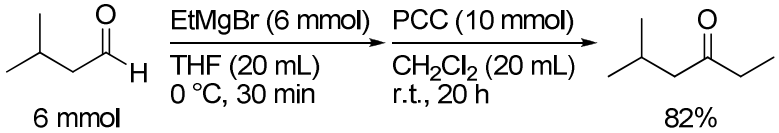
To a solution of EtMgBr, generated *in situ* from EtBr (2.2 g, MW: 108.97, 20 mmol) and Mg (0.5 g, MW: 24.31, 20 mmol) in THF (20 mL), was added cyclohexylaldehyde (2.8 g, MW: 112.17, 25 mmol) at – 20 °C under a nitrogen atmosphere for 5 min. The resulting mixture was quenched with 1 *N* HCl *aq.*, extracted with EtOAc (3 × 50 mL), dried over $MgSO_4$, and concentrated to give 1-cyclohexylpropan-1-ol (2.66 g, MW: 142.24, 94%). Spectroscopic data for this compound matched the previously reported literature values.[11] ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 0.93–1.79 (m, 17H), 3.25–3.30 (m, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 10.2, 26.2, 26.4, 26.6, 26.8, 27.7, 29.3, 43.1, 77.6.



Oxidation of the alcohol to ketone (**1i**) was prepared according to literature procedure.[12] To an oven-dried flask equipped with a stir bar was added 30 mL of dry CH_2Cl_2, the alcohol (330.7 mg, MW: 142.24, 2.32 mmol), and pyridinium chlorochromate (PCC) (1.5 g, MW: 215.56, 6.96 mmol). This dark mixture was stirred at room temperature for 2 h and quenched with

saturated NH_4Cl (50 mL). The layers were separated and the aqueous layer extracted with ether (2 × 50 mL). The combined organic phase was dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to remove the solvent. Silica gel column chromatography (hexane:ether = 5:1) provided the ketone **1i** (318.7 mg, FW: 140.22, 2.27 mmol, 98%). Spectroscopic data for this compound matched the previously reported literature values.[11] ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.03 (t, J = 7.3 Hz, 3H), 1.17–1.38 (m, 5H), 1.65–1.84 (m, 5H), 2.30–2.37 (m, 1H), 2.45 (q, J = 7.3 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 7.78, 25.7, 25.9, 28.6, 33.7, 50.6, 214.8.

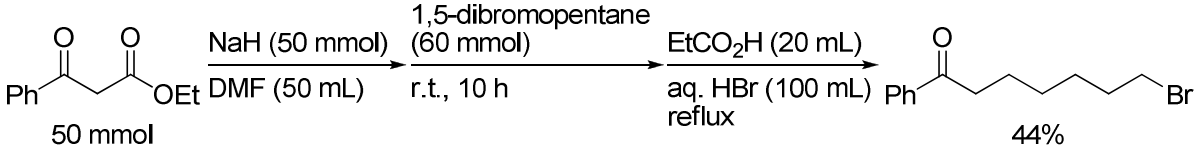
5-Methylhexan-3-one (**1i**, entry 8, Table 2) [CAS No. 623-56-3]



To a solution of EtMgBr, generated *in situ* from EtBr (0.65 g, MW: 108.97, 6.0 mmol) and Mg (0.15 g, MW: 24.31, 6.2 mmol) in THF (20 mL), was added 3-methylbutanal (0.53 g, MW: 86.13, 6.2 mmol) at 0 °C under a nitrogen atmosphere for 5 min. The resulting mixture was quenched with 1 *N* HCl *aq.*, extracted with EtOAc (3 × 50 mL), dried over $MgSO_4$, and concentrated to reduce the volume of the solution to c.a. 20 mL.

Oxidation of alcohol to ketone was prepared according to literature procedure.[11] To an oven-dried flask equipped with a stir bar was added 20 mL of dry CH_2Cl_2, the solution of the alcohol and pyridinium chlorochromate (PCC) (1.5 g, MW: 215.56, 6.96 mmol). This dark mixture was stirred at room temperature for 20 h and quenched with saturated NH_4Cl (50 mL). The layers were separated and the aqueous layer extracted with ether (2 × 50 mL). The combined organic phase was dried over anhydrous $MgSO_4$. Distillation provided the ketone (560.1 mg, FW: 114.19, 4.91 mmol, 82%). Bp 135 °C/760 mmHg. Spectroscopic data for this compound matched the previously known values.[13] ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 0.91 (d, J = 6.4 Hz, 6H), 1.05 (t, J = 7.4 Hz, 3H), 2.14 (sept, J = 6.7 Hz, 1H), 2.28 (d, J = 6.8 Hz, 2H), 2.40 (q, J = 7.3 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 7.76, 22.6, 24.7, 36.4, 51.4, 211.6.

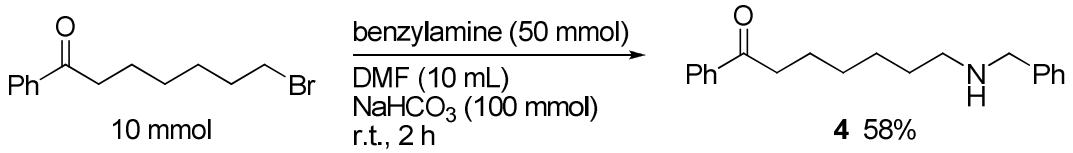
7-Bromo-1-phenylheptan-1-one [CAS No. 65542-33-8].



The titled bromide was prepared from keto ester and dibromide according to the literature procedure.[14] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40–1.54 (m, 4H), 1.76 (quint., 7.2 Hz, 2H), 1.88 (quint., 7.2 Hz, 2H), 2.98 (t, 7.1 Hz, 2H), 3.42 (t, J = 7.1 Hz, 2H), 7.46 (t, J = 7.3 Hz, 2H), 7.56 (t, 7.3 Hz, 1H), 7.96 (d, 7.3 Hz,2H), 7.95 (d, 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.0, 28.0, 28.4, 32.6, 33.9,

38.4, 128.0, 128.6, 132.9, 137.0, 200.3;

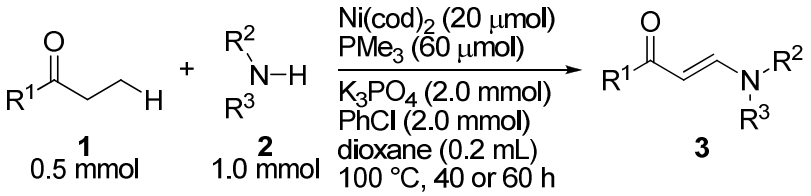
7-Benzylamino-1-phenylheptan-1-one (**4**, Eq 1).



The titled amide **4** was prepared from bromide and benzylamine according to the literature procedure.[14] Mp 65.9–66.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.37–1.55 (m, 8H), 1.74 (t, 7.2 Hz, 2H), 2.63 (t, 7.2 Hz, 2H), 2.96 (t, 2.4 Hz, 2H), 3.79 (s, 2H), 7.26–7.33 (m, 6H), 7.46 (t, 7.6 Hz, 2H), 7.55 (t, 7.4 Hz, 1H), 7.95 (d, 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 38.5, 49.4, 54.1, 126.8, 128.0, 128.1, 128.3, 128.5, 132.8, 137.0, 140.5, 200.4; ; IR (neat) 3029 w, 2928 s, 2855 s, 1683 s, 1590 w, 1452 m, 1361 m, 1216 w, 1117 w, 973 w, 738 m, 695 m cm^{-1}; MS *m*/*z* (%, relative intensity) 295 (M^+, 5), 281 (5), 204 (21), 190 (19), 176 (38), 160 (11), 146 (13), 133 (16), 120 (58), 105 (51), 91 (100), 77 (60); Anal. Calcd for $C_{14}H_{17}NO_3$: C, 81.31; H, 8.53; N, 4.74. Found: C, 81.11; H, 8.50; N, 4.82.

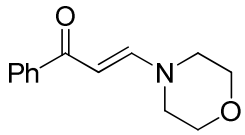
III. Reaction of 1 with Amines 2 (Table 1, Table 2, eq 2).

General Procedure:



In a nitrogen-filled drybox, a 4 mL screw-capped vial was charged with $Ni(cod)_2$ (5.5 mg, MW: 275.06, 0.02 mmol), K_3PO_4 (424.5 mg, MW: 212.27, 2.0 mmol), dioxane (0.2 mL). After a magnetic stir bar was added, the vial was fitted with a septum cap, and removed from dry box. A THF solution of PMe_3 (60 μL, 1 M THF solution, 0.06 mmol), chlorobenzene (0.2 mL, MW: 112.56, *d* 1.106 g/mL, 1.97 mmol), amine (1.0 mmol), and ethyl ketone (0.5 mmol) were added. The resulting mixture was heated at 100 °C. The progress of the reaction was confirmed by GC analysis. After completely consumption of the starting material, the reaction mixture was diluted with water (1 mL) and extracted with EtOAc (3 × 1 mL). The organic layer was concentrated, and purified by silica gel column chromatography (hexane:EtOAc).

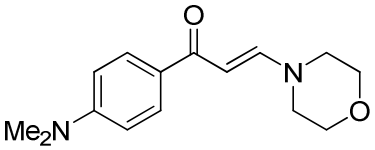
(*E*)-3-Morpholino-1-phenylprop-2-en-1-one (**3a**, Table 1, entry 1) [CAS No. 25039-19-4].



The compound was prepared according to the General Procedure with propiophenone (68.8 mg, MW: 134.18, 0.513 mmol) and morpholine (88 μL,

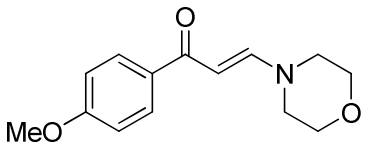
MW: 87.12, *d* 0.996 g/mL, 1.0 mmol) for 40 h. After purification by silica gel column chromatography (hexane:EtOAc = 1:1 to 1:6), **3a** was obtained as a pale yellow solid (95.7 mg, MW: 217.26, 0.440 mmol, 86%). R_f = 0.25 (hexane:EtOAc = 1:6); Mp 90.6–91.1 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.38 (t, *J* = 4.9 Hz, 4H), 3.74 (t, *J* = 4.9 Hz, 4H), 5.88 (d, *J* = 12.6 Hz, 1H), 7.39–7.49 (m, 3H), 7.72 (d, *J* = 12.6 Hz, 1H), 7.88 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 48.5 (brs),[15] 66.1, 92.4, 127.4, 128.1, 131.1, 140.1, 152.6, 189.0; IR (neat) 2967 w, 2905 w, 2855 w, 1640 s, 1548 s, 1442 m, 1370 m, 1278 m, 1209 s, 1112 m, 1061 w, 1016 m, 924 w, 882 w, 762 w, 706 m, 659 w, 617 w, 555 w cm^{-1}; MS *m*/*z* (%, relative intensity) 217 (M^+, 92), 200 (95), 170 (73), 159 (46), 144 (22), 140 (46), 131 (89), 112 (57), 105 (88), 103 (22), 91 (73), 86 (58), 85 (32), 82 (100), 80 (30), 78 (34), 77 (99), 68 (20), 67 (20), 65 (25), 56 (31), 55 (75), 54 (38), 53 (29), 51 (60), 50 (22); HRMS Calcd for [$C_{13}H_{15}NO_2$+H^+]: 218.1181, Found: 218.1173.

(*E*)-1-[4-(Dimethylamino)phenyl]-3-morpholinoprop-2-en-1-one (**3b**, Table 2, entry 1).



The compound was prepared according to the General Procedure with 1-[4-(dimethylamino)phenyl]propan-1-one (47.1 mg, MW: 177.24, 0.27 mmol) and morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL, 1.0 mmol) for 60 h. After purification by silica gel column chromatography (EtOAc), **3b** was obtained as a yellow solid (55.7 mg, MW: 260.33, 0.21 mmol, 80%). R_f = 0.11 (EtOAc); Mp 127.0–127.1 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.02 (s, 6H), 3.34 (t, *J* = 4.8 Hz, 4H), 3.73 (t, *J* = 4.8 Hz, 4H), 5.91 (d, *J* = 12.8 Hz, 1H), 6.66 (d. *J* = 6.6 Hz, 2H), 7.67 (*J* = 12.8 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.0, 49.0 (brs),[15] 66.2, 92.2, 110.7, 127.5, 129.4, 151.6, 152.5, 187.5; IR (neat) 3451 w, 2859 m, 1595 s, 1364 s, 1173 s, 1012 m, 923 w, 731 w cm^{-1}; MS *m*/*z* (%, relative intensity) 261 (M^+, 24), 260 (39), 243 (45), 213 (35), 175 (28), 174 (39), 149 (21), 148 (100), 134 (77), 112 (24), 87 (23), 86 (21), 82 (69), 77 (35); HRMS Calcd for [$C_{15}H_{20}N_2O_2$+H^+]: 261.1603, Found: 261.1602.

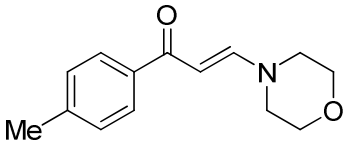
(*E*)-1-(4-methoxyphenyl)-3-morpholinoprop-2-en-1-one (**3c**, Table 2, entry 2) [CAS No. 71035-25-1].



The compound was prepared according to the General Procedure with 1-(4-methoxyphenyl)propan-1-one (81.9 mg, MW: 164.20, 0.499 mmol) and morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL, 1.0 mmol) for 60 h. After purification by silica gel column chromatography (hexane:EtOAc 1:1, then EtOAc only), **3c** was obtained as a pale yellow solid (114.1 mg, MW: 247.29, 0.462 mmol,

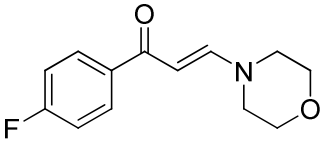
93%). Mp 86.0–86.1 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.35–3.38 (m, 4H), 3.72–3.75 (m, 4H), 3.84 (s, 3H), 5.87 (d, *J* = 12.8 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.70 (d, *J* = 12.8 Hz, 2H), 7.89 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 49.3 (brs),[15] 55.2, 66.1, 91.9, 113.2, 129.4, 132.7, 152.2, 162.0, 187.7; IR (neat) 2852 w, 1638 s, 1591 s, 1547 s, 1445 m, 1367 s, 1256 s, 1213 s, 1169 s, 1114 m, 1019 m, 785 w, 625 w cm^{-1}; MS *m*/*z* (%, relative intensity) 247 (M^+, 62), 231 (46), 230 (81), 200 (63), 189 (34), 188 (26), 175 (22), 174 (50), 162 (52), 161 (58), 160 (31), 147 (46), 146 (30), 136 (23), 135 (92), 134 (21), 122 (12), 121 (74), 112 (55), 110 (38), 92 (48), 91 (21), 86 (27), 82 (100), 81 (25), 77 (76), 64 (33), 63 (28), 56 (22), 55 (48), 54 (25), 53 (23); Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.84; H, 6.89; N, 5.57.

(*E*)-3-morpholino-1-*p*-tolylprop-2-en-1-one (**3d**, Table 2, entry 3) [CAS No. 71035-24-0]



The compound was prepared according to the General Procedure with 1-*p*-tolylpropan-1-one (69.5 mg, MW: 148.20, 0.469 mmol) and morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL, 1.0 mmol) for 40 h. After purification by silica gel column chromatography (hexane:EtOAc = 1:7), **3d** was isolated as a pale yellow oil (106.5 mg, MW: 231.29, 0.461 mmol, 98%). R_f = 0.27 (hexane:EtOAc = 1:7); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.37 (s, 3H), 3.33–3.36 (m, 4H), 3.69–3.73 (m, 4H), 5.87 (d, *J* = 12.4 Hz, 1H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.70 (d, *J* = 12.4 H, 1H), 7.80 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 48.6 (brs),[15] 66.0, 92.1, 127.4, 128.7, 137.2, 141.4, 152.4, 188.5; IR (neat) 3472 w, 2966 m, 2910 m, 2856 m, 1644 s, 1555 s, 1444 m, 1372 s, 1283 m, 1211 m, 1173 m, 1016 m, 775 m, 448 m cm^{-1}; MS *m*/*z* (%, relative intensity) 232 (52), 231 (76), 230 (27), 215 (59), 214 (87), 200 (26), 186 (29), 185 (29), 184 (68), 174 (31), 173 (49), 172 (40), 159 (21), 158 (57), 146 (54), 145 (66), 144 (43), 140 (37), 131 (59), 130 (23), 119 (82), 115 (24), 112 (55), 105 (65), 91 (87), 89 (21), 86 (72), 85 (37), 82 (100), 72 (46), 68 (20), 65 (69), 63 (25), 57 (22), 56 (31), 55 (65), 54 (35), 53 (27); HRMS Calcd for [$C_{14}H_{17}NO_2$+H^+]: 232.1338, Found: 232.1339.

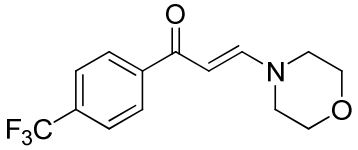
(*E*)-1-(4-fluorophenyl)-3-morpholinoprop-2-en-1-one (**3e**, Table 2, entry 4) [CAS No. 15395-92-2].



The compound was prepared according to the General Procedure with 1-(4-fluorophenyl)propan-1-one (78.7 mg, MW: 152.17, 0.517 mmol) and morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL, 1.0 mmol) for 60 h. After purification by silica gel column chromatography (hexane:EtOAc = 5:1 then 1:5), **3e** was obtained as a pale yellow solid (94.7 mg, MW: 235.25, 0.403 mmol, 78%). R_f = 0.33 (hexane:EtOAc= 1:5); Mp 78.9–79.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.36–3.41 (m, 4H),

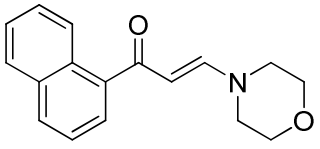
3.70–3.77 (m, 4H), 5.83 (d, J = 12.4 Hz, 1H), 7.05–7.10 (m, 2H), 7.73 (d, J = 12.4 Hz, 1H), 7.88–7.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 48.6 (brs),[15] 66.1, 91.7, 114.9 (d, J = 21.5 Hz), 129.7 (d, J = 8.9 Hz), 136.2 (d, J = 2.8 Hz), 152.7, 164.5 (d, J = 251.1 Hz), 187.3; IR (neat) 2968 w, 2857 w, 1644 s, 1600 s, 1555 s, 1369 m, 1217 s, 1114 m, 1017 m, 781 m, 469 m cm^{-1}; MS m/z (%, relative intensity) 235 (82), 234 (25), 219 (63), 218 (90), 204 (21), 190 (25), 189 (24), 188 (70), 178 (55), 177 (63), 176 (55), 164 (31), 163 (28), 162 (31), 150 (65), 149 (83), 148 (65), 140 (28), 123 (89), 122 (25), 112 (62), 109 (72), 96 (27), 95 (87), 94 (29), 89 (25), 86 (47), 85 (41), 83 (23), 82 (100), 75 (78), 74 (27), 70 (22), 69 (23), 68 (28), 57 (26), 56 (38), 55 (74), 54 (46), 53 (33); Anal. Calcd for $C_{13}H_{14}FNO_2$: C, 66.37; H, 6.00; N, 5.95. Found: C, 66.29; H, 6.02; N, 5.95.

(*E*)-3-morpholino-1-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (**3f**, Table 2, entry 5).



The compound was prepared according to the General Procedure with 1-(4-(trifluoromethyl)phenyl)propan-1-one (98.2 mg, MW: 202.17, 0.486 mmol) and morpholine (88 μL, MW: 87.12, d 0.996 g/mL, 1.0 mmol) for 40 h. After purification by silica gel column chromatography (hexane:EtOAc = 1:2), **3f** was obtained as a pale yellow solid (96.9 mg, MW: 285.26, 0.34 mmol, 70%). R_f = 0.22 (hexane:EtOAc = 1:2); Mp 105.5–105.6 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.40–3.42 (m, 4H), 3.72–3.75 (m, 4H), 5.86 (d, J = 12.4 Hz, 1H), 7.66 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 12.4 Hz, 1H), 7.98 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.8 (brs, NCH_2),[15] 52.9 (brs, NCH_2),[15] 65.9, 91.7, 123.7 (q, J = 272.4 Hz), 124.9 (q, J = 3.6 Hz), 127.5, 132.0 (q, J = 32.3 Hz), 143.1, 153.1, 187.1; IR (neat) 3436 w, 2972 w, 2857 w, 1641 m, 1547 s, 1322 s, 1113 s, 1067 m, 1014 m, 734 m cm^{-1}; MS m/z (%, relative intensity) 286 (68), 285 (85), 284 (39), 269 (58), 268 (80), 238 (63), 228 (63), 227 (50), 226 (43), 212 (29), 200 (48), 199 (68), 198 (58), 174 (27), 173 (82), 172 (33), 159 (72), 158 (68), 151 (29), 146 (25), 145 (86), 143 (37), 140 (56), 131 (73), 130 (29), 125 (23), 112 (73), 95 (34), 94 (21), 86 (73), 85 (51), 83 (24) 82 (100), 81 (22),, 75 (46), 70 (24), 69 (27), 68 (28), 67 (24), 57 (32), 56 (49), 55 (77), 54 (58), 53 (40), 50 (21); Anal. Calcd for $C_{14}H_{14}F_3NO_2$: C, 58.95; H, 4.95; N, 4.91. Found: C, 59.00; H, 5.00; N, 4.93.

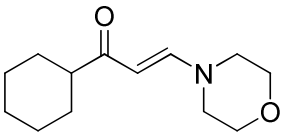
(*E*)-3-morpholino-1-(naphthalen-1-yl)prop-2-en-1-one (**3g**, Table 2, entry 6).



The compound was prepared according to the General Procedure with 1-(naphthalen-1-yl)propan-1-one (96.1 mg, MW: 184.23, 0.522 mmol) and morpholine (88 μL, MW: 87.12, d 0.996 g/mL, 1.0 mmol) for 60 h. After purification by silica gel column chromatography (hexane:EtOAc = 2:1), **3g** was

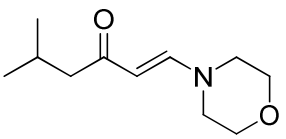
isolated as a pale yellow oil (117.6 mg, MW: 267.32, 0.44 mmol, 84%). R_f = 0.18 (hexane:EtOAc = 2:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.33 (t, *J* = 4.9 Hz, 4H), 3.74 (t, *J* = 4.9 Hz, 4H), 5.67 (d, *J* = 12.8 Hz, 1H), 7.44–7.59 (m, 5H), 7.86 (m, 2H), 8.26 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 46.0 (brs, N*C*H$_2$),[15] 52.0 (brs, N*C*H$_2$),[15] 65.9, 98.3, 124.5, 124.9, 125.8, 125.9, 126.4, 128.0, 129.4, 130.2, 133.5, 139.7, 153.3, 193.8; IR (neat) 2855 m, 1638 s, 1550 s, 1441 s, 1360 s, 1277 s, 1226 s, 1112 s, 1018 m, 788 m, 732 m cm^{-1}; MS *m*/*z* (%, relative intensity) 267 (M^+, 40), 183 (29), 182 (100), 181 (100), 180 (37), 165 (51), 155 (59), 154 (31), 153 (36), 152 (52), 141 (64), 140 (45), 127 (100), 126 (28), 90 (239), 86 (100), 82 (90), 77 (40), 76 (28), 56 (21), 55 (35); HRMS Calcd for [$C_{17}H_{17}NO_2$+H^+]: 268.1338, Found: 268.1324.

(*E*)-1-cyclohexyl-3-morpholinoprop-2-en-1-one (**3h**, Table 2, entry 7).



The compound was prepared according to the General Procedure with 1-cyclohexylpropan-1-one (61.5 mg, MW: 140.22. 0.439 mmol) and morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL, 1.0 mmol) for 60 h. After purification by silica gel column chromatography (hexane:EtOAc = 1:1 to 1:5), **3h** was isolated as a pale yellow solid (51.5 mg, MW: 223.31, 0.231 mmol, 53%). R_f = 0.23 (hexane:EtOAc = 1:5); Mp 56.7–56.8 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.10–1.44 (m, 5H), 1.65–1.71 (m, 2H), 1.78–1.82 (m, 3H), 2.23–2.31 (m, 1H), 3.28 (t, *J* = 4.8 Hz, 4H), 3.72 (t, *J* = 4.8 Hz, 4H), 5.21 (d, *J* = 12.8 Hz, 1H), 7.48 (d, *J* = 12.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.3, 29.5, 50.4, 66.2, 94.6, 150.9, 201.9 (a peak of α-carbon of the amine unit could not be observed[15]); IR (neat) 2925 m, 2852 w, 1654 w, 1566 s, 1443 m, 1372 m, 1292 m, 1112 m, 1016 w cm^{-1}; MS *m*/*z* (%, relative intensity) 223 (M^+, 47), 141 (43), 140 (100), 94 (35), 82 (47), 67 (29), 55 (59), 54 (21); Anal. Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 69.79; H, 9.40; N, 6.21.

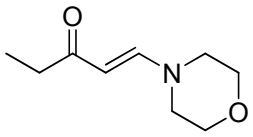
(*E*)-5-methyl-1-morpholinohex-1-en-3-one (**3i**, Table 2, entry 8).



The compound was prepared according to the General Procedure with 5-Methylhexan-3-one (19.9 mg, MW: 114.19. 0.174 mmol) and morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL, 1.0 mmol) for 40 h. After purification by silica gel column chromatography (hexane:EtOAc = 3:1 to 1:3), **3i** was isolated as a pale yellow solid (18.7 mg, MW: 197.27, 0.095 mmol, 54%). R_f = 0.31 (hexane:EtOAc = 1:6); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.934 (d, *J* = 6.8 Hz, 6H), 2.13 (sept, *J* = 6.8 Hz, 1H), 2.22 (d, *J* = 6.8 Hz, 2H), 3.28 (t, *J* = 4.8 Hz, 4H), 3.72 (t, *J* = 4.8 Hz, 4H), 5.19 (d, *J* = 13.0 Hz, 1H), 7.44 (d, *J* = 13.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.2, 26.5, 51.7, 66.6, 97.2, 151.2, 198.9 (a peak of α-carbon of

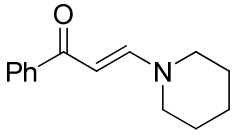
the amine unit could not be observed[15]); IR (neat) 2956 s, 2861 m, 1654 m, 1567 s, 1444 m, 1369 m, 1284 w, 1229 w, 1161 w, 1114 m, 1072 w, 1017 w cm^{-1}; MS *m*/*z* (%, relative intensity) 197 (M^+, 63), 182 (12), 155 (43), 140 (100), 113 (46), 94 (36), 82 (68), 67 (29), 55 (60); HRMS Calcd for [$C_{11}H_{19}O_2N+H^+$]: 198.1494, Found: 198.1465.

(*E*)-1-morpholinopent-1-en-3-one (ref. 12) [CAS No. 73813-03-3].



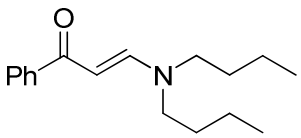
The compound was prepared according to the General Procedure with pentan-3-one (MW: 86.13, 42.4 mg, 0.492 mmol) and morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL, 1.0 mmol) for 40 h. After purification by silica gel column chromatography (hexane:EtOAc = 1:1, then EtOAc:MeOH = 8:1), (*E*)-1-morpholinopent-1-en-3-one was isolated as a yellow oil (28.6 mg, MW: 169.22, 0.169 mmol, 34%). R_f = 0.28 (EtOAc:MeOH = 8:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.11 (t, *J* = 7.5 Hz, 3H), 2.37 (q, *J* = 7.5 Hz, 2H), 3.28 (t, *J* = 4.8 Hz, 4H), 3.72 (t, *J* = 4.8 Hz, 4H), 5.20 (d, *J* = 12.8 Hz 1H), 7.45 (d, *J* = 12.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 9.45, 34.6, 49.1 (brs),[15] 66.1, 99.5, 150.6, 199.3; IR (neat) 3421 w, 2968 w , 2923 w, 2857 w, 1655 m, 1612 m, 1569 s, 1445 w, 1372 w, 1290 w, 1227 w, 1115 w, 1014 w cm^{-1}; MS *m*/*z* (%, relative intensity) 169 (M^+, 34), 140 (100), 82 (56), 55 (32); HRMS Calcd for [$C_9H_{15}NO_2+H^+$]: 170.1181, Found: 170.1176.

(*E*)-1-phenyl-3-(piperidin-1-yl)prop-2-en-1-one (**3j**, Table 2, entry 9) [CAS No. 3506-37-4]



The compound was prepared according to the General Procedure with propiophenone (67.6 mg, MW: 134.18, 0.504 mmol) and piperidine (1.0 mmol, MW: 85.15, 85.1 mg) for 40 h. After purification by silica gel column chromatography (hexane:EtOAc 7:1 to 1:5), **3j** was obtained as a pale yellow solid (92.6 mg, MW: 215.29, 0.431 mmol, 85%). R_f = 0.34 (hexane:EtOAc = 1:7); Mp 89.1–89.8 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.67 (brs, 6H), 3.36 (brs 4H), 5.82 (d, *J* = 12.4 Hz, 1H), 7.78 (d, *J* = 12.4 Hz, 1H), 7.88 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.0, 26.0 (brs),[15] 46.3 (brs, N*C*H_2),[15] 54.9 (brs, N*C*H_2),[15] 91.2, 127.4, 128.0, 130.7, 140.7, 153.0, 189.0; IR (neat) 2936 w, 2855 w, 1639 s, 1547 s, 1450 m, 1370 m, 1280 m, 1209 m, 1055 w, 994 w, 956 w cm^{-1}; MS *m*/*z* (%, relative intensity) 215 (47), 198 (100), 138 (24), 131 (24), 110 (44), 105 (48), 84 (65), 83 (52), 82 (44), 77 (78), 55 (34); Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.16; H, 7.94; N, 6.47.

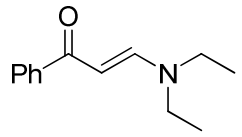
(*E*)-3-(dibutylamino)-1-phenylprop-2-en-1-one (**3k**, Table 2, entry 10) [CAS No. 56570-57-1]



The compound was prepared according to the General Procedure with

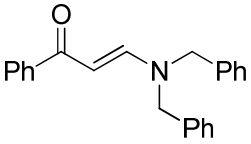
propiophenone (67.3 mg, MW: 134.18, 0.502 mmol) and dibutylamine (1.0 mmol, MW: 129.24, 129.2 mg) for 40 h. After purification by silica gel column chromatography (hexane:EtOAc = 5:1 to 1:5), **3k** was isolated as a pale yellow oil (100.6 mg, MW: 259.39, 0.388 mmol, 77%). R_f = 0.26 (hexane:EtOAc = 3:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.97 (s, 6H), 1.35 (s, 4H), 1.61 (s, 4H), 3.25 (s, 4H), 5.74 (d, *J* = 12.4 Hz, 1H), 7.38–7.45 (m, 3H), 7.80 (d, *J* = 12.4 Hz, 1H), 7.87 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.7 (2 × *C*H$_3$), 19.7, 20.2, 28.4, 31.3, 48.4, 56.2, 91.7, 127.4, 128.0, 130.6, 140.8, 153.2, 188.6; IR (neat) 2953 m, 2872 w, 1640 m, 1549 s, 1460 m, 1366 m, 1285 m, 1204 m, 1049 w cm^{-1}; HRMS Calcd for [$C_{17}H_{26}NO$+H$^+$]: 260.2014, Found: 260.2013.

(*E*)-3-(diethylamino)-1-phenylprop-2-en-1-one (**3l**, Table 2, entry 11) [CAS No. 23674-58-0].



The compound was prepared according to the General Procedure with propiophenone (66.6 mg, MW: 134.18, 0.496 mmol) and diethylamine (1.0 mmol, MW: 73.14, 73.1 mg) for 60 h. After purification by silica gel column chromatography (hexane:EtOAc = 1:1 to 1:8), **3l** was obtained as a pale yellow oil (58.4 mg, MW: 203.28, 0.288 mmol, 58%). R_f = 0.21 (hexane:EtOAc = 1:8); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.25 (t, *J* = 6.8 Hz, 6H), 3.34 (t, *J* = 6.8 Hz, 4H), 5.77 (d, *J* = 12.6 Hz, 1H), 7.38–7.47 (m, 3H), 7.82 (d, *J* = 12.6 Hz, 1H), 7.89 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.5 (brs),[15] 14.7 (brs),[15] 42.8 (brs),[15] 50.5 (brs),[15] 91.6, 127.4, 128.0, 130.7, 140.7, 152.3, 188.7; IR (neat) 2976 w, 1639 s, 1548 s, 1465 m, 1365 s, 1280 m, 1219 m, 1126 w, 1052 m, 989 w, 760 w, 706 w cm^{-1}; MS *m*/*z* (%, relative intensity) 203 (M$^+$, 79), 187 (29), 186 (88), 174 (59), 156 (23), 146 (31), 131 (23), 126 (34), 105 (97), 98 (71), 96 (28), 91 (59), 78 (23), 77 (100), 72 (27), 70 (55), 68 (26), 56 (73), 55 (23), 51 (32); Anal Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.73; H, 8.49; N, 6.88.

(*E*)-3-(dibenzylamino)-1-phenylprop-2-en-1-one (**3m**, Table 2, entry 12).

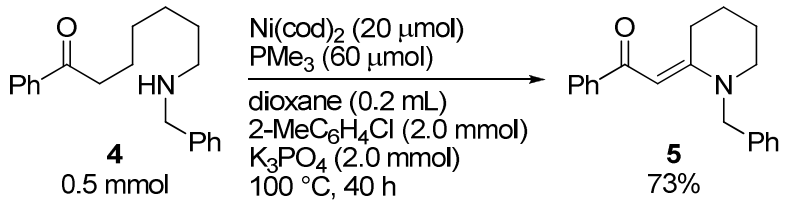


The compound was prepared according to the General Procedure with propiophenone (66.4 mg, MW: 134.18, 0.495 mmol) and dibenzylamine (1.0 mmol, MW: 197.28, 197.3 mg) for 40 h. After purification by silica gel column chromatography (hexane:EtOAc 5:1 to 1:1,), **3m** was isolated as a yellow solid (MW: 327.42, 121.9 mg, 0.373 mmol, 75%). R_f = 0.16 (hexane:EtOAc = 1:1); Mp 105.2–105.3 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.43 (br, 2H), 6.01 (d, *J* = 12.0 Hz, 1H), 7.20–7.45 (m, 13H), 7.85 (d, *J* = 8.0 Hz, 2H), 8.18 (d, *J* = 12.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 50.9 (brs, N*C*H$_2$),[15] 59.3 (brs, N*C*H$_2$),[15] 93.2, 127.5, 128.8, 131.0, 140.3, 154.1, 189.2 (some peaks of the amine unit could not be observed.[15]); IR (neat) 3032 w, 1640 s, 1546 s, 1446 m, 1362 s, 1282 m, 1195 m, 1048 w, 903 w,

749 m, 701 m cm^{-1}; MS *m*/*z* (%, relative intensity) 327 (M^+, 30), 237 (32), 236 (100), 167 (64), 105 (100), 103 (23), 92 (26), 91 (97), 77 (81), 65 (70); Anal. Calcd for $C_{23}H_{21}NO$: C, 84.37; H, 6.46; N, 4.28; O, 4.89. Found: C, 84.11; H, 6.51; N, 4.30.

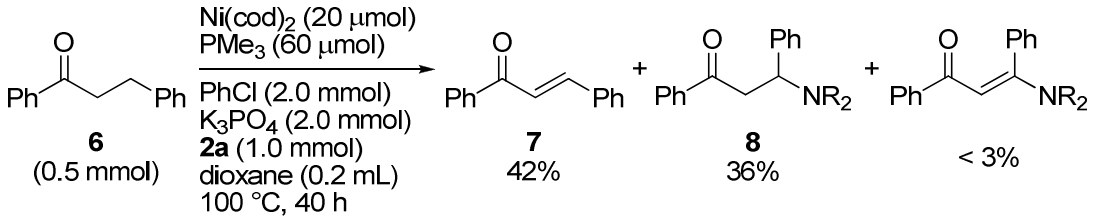
IV. Intramolecular Reaction of 4 (Eq. 1)

(*E*)-2-(1-benzylpiperidin-2-ylidene)-1-phenylethanone (5, Eq. 1)



The compound **4** was prepared according to the General Procedure with 7-(benzylamino)-1-phenylheptan-1-one (**5**) (137.4 mg, MW: 295.42, 0.465 mmol) in 2-chlorotoluene as an oxidant for 40 h. After purification by silica gel column chromatography (benzene:dioxane 20:1 to 10:1), the cyclic enaminone **5** was isolated as a pale yellow solid (MW: 291.39, 97.2 mg, 0.334 mmol, 72%). R_f = 0.21 (benzene:dioxane = 20:1); Mp 130.2–130.9 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.76–1.91 (m, 4H), 3.41–3.47 (m, 4H), 4.57 (s, 2H), 5.78 (s, 1H), 7.22–7.40 (m, 8H), 7.64 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.5, 23.1, 28.4, 50.7, 55.9, 91.6, 126.5, 127.2, 127.5, 127.9, 128.9, 130.0, 135.7, 142.9, 164.8, 187.9; IR (neat) 3056 w, 2941 w, 2861 w, 1613 w, 1573 w, 1529 s, 1477 m, 1354 w, 1331 w, 1271 w, 1217 m, 1172 m, 1059 w, 876 w, 760 w, 730 w, 700 w cm^{-1}; MS *m*/*z* (%, relative intensity) 291 (M^+, 11), 274 (52), 186 (75), 105 (31), 91 (100), 65 (26); HRMS Calcd for [$C_{20}H_{21}NO+H^+$]: 292.1701, Found: 292.1703.; Anal. Calcd for $C_{23}H_{21}NO$: C, 82.44; H, 7.26; N, 4.81; O, 5.49. Found: C, 82.28; H, 7.21; N, 4.81.

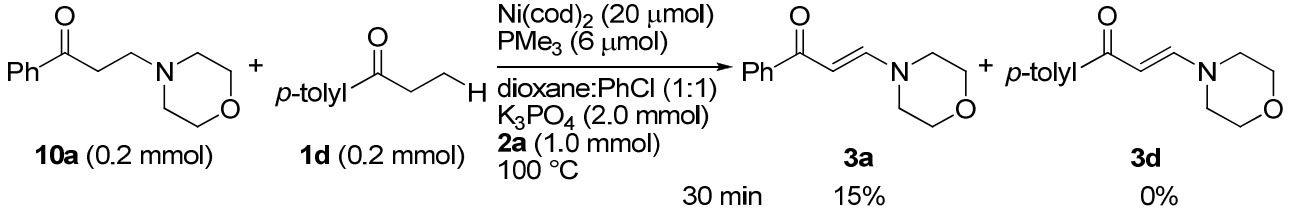
V. Reaction of 6 with 2a (Eq. 2)



The titled reaction was carried out according to the General Procedure with 1,3-diphenylpropan-1-one (**6**) (98.0 mg, MW: 210.27, 0.466 mmol) and morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL, 1.0 mmol) for 40 h. After purification by silica gel column chromatography (hexane:EtOAc 20:1 to 2:1,), **7** and **8** were isolated as white solids. Spectroscopic data for **7** and **8** matched the previously reported literature values.[3] The corresponding enaminone was

detected as a small peak by GC and GC–MS analyses.

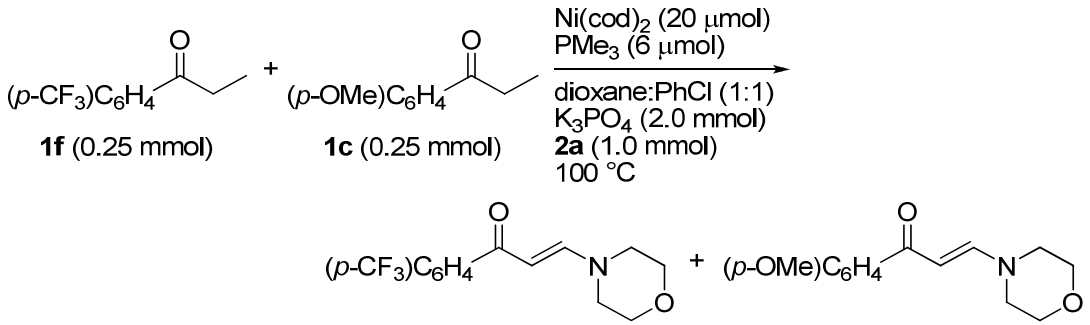
VI. Competitive Reaction between 10a and 1d with 2a (Scheme 2).



	3a	3d
30 min	15%	0%
4 h	78%	4%
20 h	83%	46%
40 h	83%	67%

In a nitrogen-filled drybox, a 4 mL screw-capped vial was charged with $Ni(cod)_2$ (5.5 mg, MW: 275.06, 0.02 mmol), K_3PO_4 (424.5 mg, MW: 212.27, 2.0 mmol), and dioxane (0.2 mL). After a magnetic stir bar was added, the vial was fitted with a septum cap, and removed from drybox. PMe_3 (60 μL, 1 M THF solution), chlorobenzene (0.2 mL, MW: 112.56, *d* 1.106, 1.97 mmol), morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL, 1.0 mmol), **10a** (41.0 mg, MW: 219.28, 0.187 mmol), and **1d** (31.3 mg, MW: 148.20, 0.211 mmol) were added. The resulting mixture was heated at 100 °C. The progress of the reaction was confirmed by GC analysis.

VII. Competitive Reaction between 1c and 1f with 2a (ref. 11).



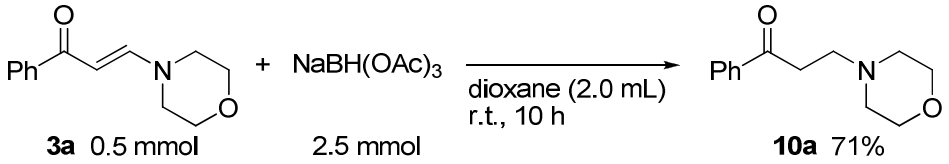
	3f	3c
30 min	15%	0%
10 h	76%	18%
20 h	99%	46%
40 h	99%	67%

In a nitrogen-filled drybox, a 4 mL screw-capped vial was charged with $Ni(cod)_2$ (5.5 mg, MW: 275.06, 0.02 mmol), K_3PO_4 (424.5 mg, MW: 212.27, 2.0 mmol), and dioxane (0.2 mL). After a magnetic stir bar was added, the screw-vial was fitted with a septum cap. The vial was removed from drybox. PMe_3 (60 μL, 1 M THF solution, 0.06 mmol), chlorobenzene (0.2 mL, MW: 112.56, *d* 1.106, 1.97 mmol), morpholine (88 μL, MW: 87.12, *d* 0.996 g/mL 1.0 mmol), **1f** (54.1 mg, MW: 202.17, 0.268 mmol), and **1c** (39.4 mg, MW: 164.20, 0.240 mmol) were added.

The resulting mixture was heated at 100 °C. The progress of the reaction was confirmed by GC analysis.

VIII. Selective Reduction of Enaminone 3a (Scheme 3).

3-morpholino-1-phenylpropan-1-one (**5**, Scheme 3) [CAS No. 2298-48-8].

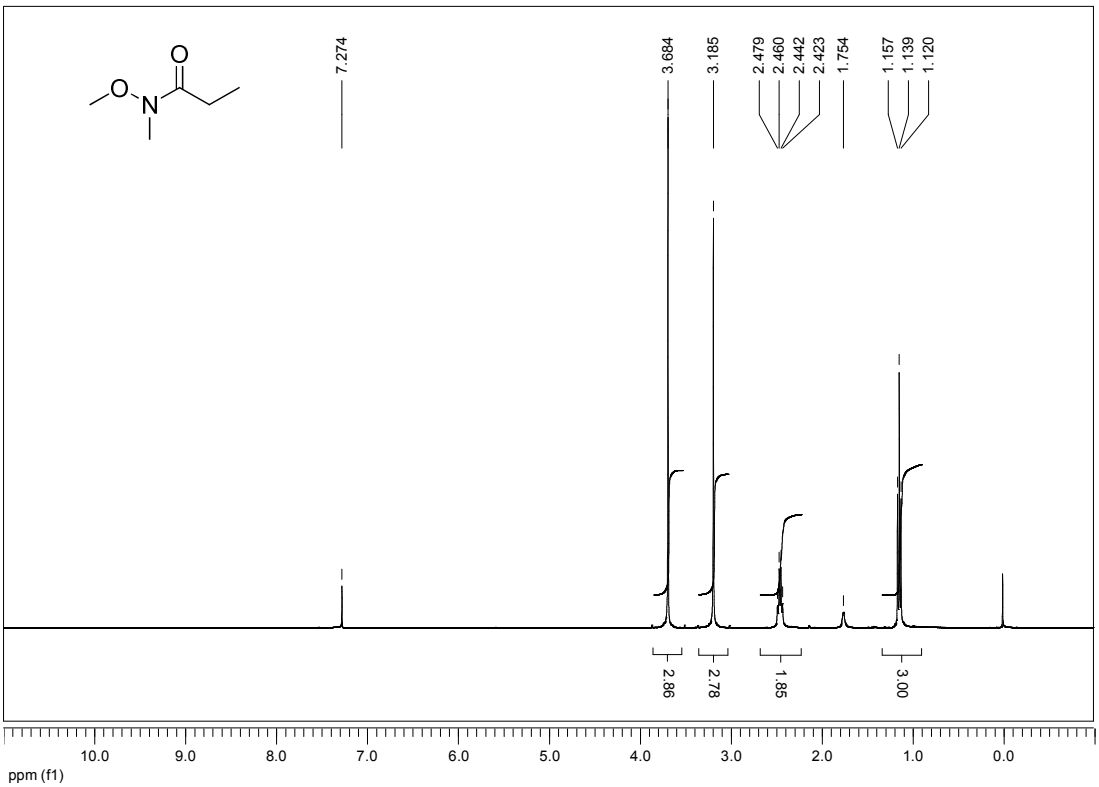


3a 0.5 mmol 2.5 mmol **10a** 71%

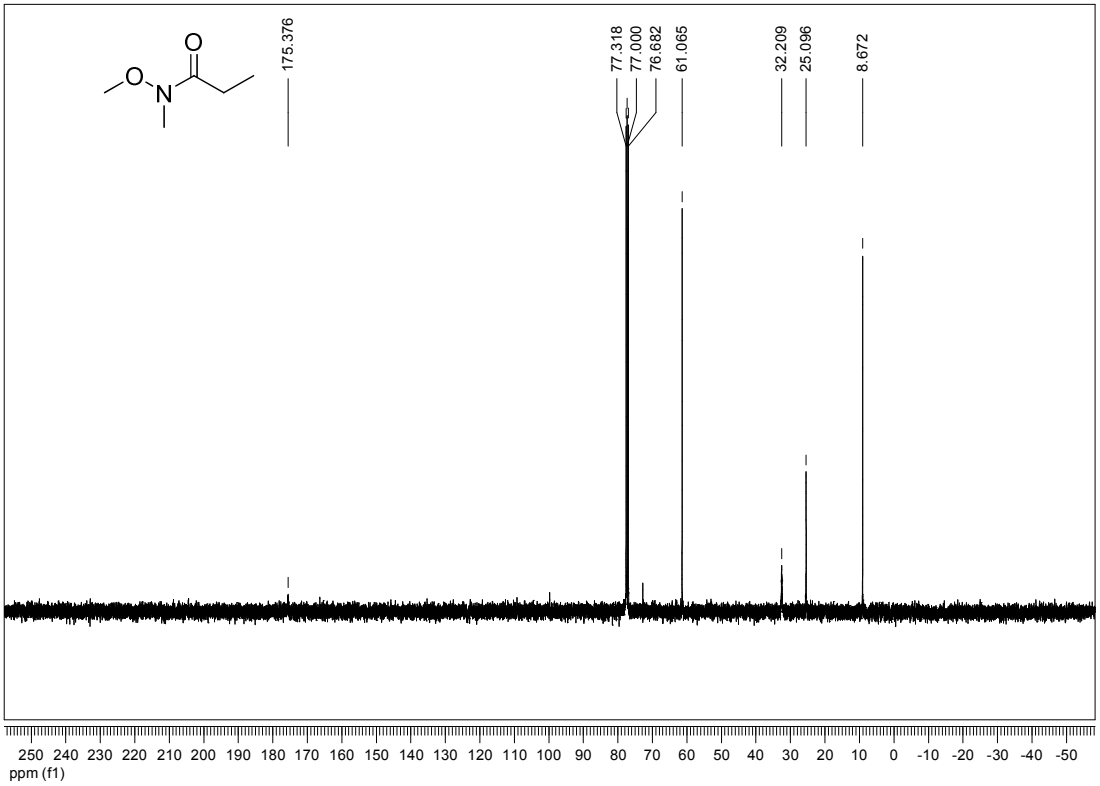
Enaminone **3a** (103.9 mg, MW: 217.26, 0.479 mmol) was placed in the round-bottomed flask. The white solid was dissolved in dioxane (2.0 mL). To the solution was slowly added $NaBH(OAc)_3$ (0.52 g, MW: 211.94, 2.5 mmol) at room temperature. The progress of the reaction was monitored by GC analyses. After 10 h, the starting material was consumed perfectly. The mixture was quenched with water (2 mL), extracted with EtOAc. The organic layer was concentrated, and the resulting residue was purified by silica gel column chromatography (EtOAc:MeOH = 1:0 to 10:1) to give colorless oil **10a** (74.8 mg, MW: 219.28, 0.342 mmol, 71%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.51 (t, J = 4.5 Hz, 4H), 2.84 (t, J = 7.4 Hz, 2H), 3.19 (t, J = 7.4 Hz, 2H), 3.72 (t, J = 4.5 Hz, 4H), 7.47 (t, J = 7.2 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.96 (d, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 36.0, 53.5, 53.7, 66.9, 128.0, 128.6, 133.1, 136.9, 198.9; IR (neat) 2952 w, 2852 m, 2810 m, 1683 s, 1589 w, 1450 m, 1365 m, 1266 m, 1212 m, 1120 s, 984 w, 865 w, 747 m, 693 m cm^{-1}; MS *m*/*z* (%, relative intensity) 219 (M^+, 4), 105 (54), 100 (100), 99 (47), 77 (78), 56 (65), 55 (20); HRMS Calcd for [$C_{13}H_{17}NO_2$+H^+]: 220.1338, Found: 220.1337.

IX. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of Starting Materials 1 and 4

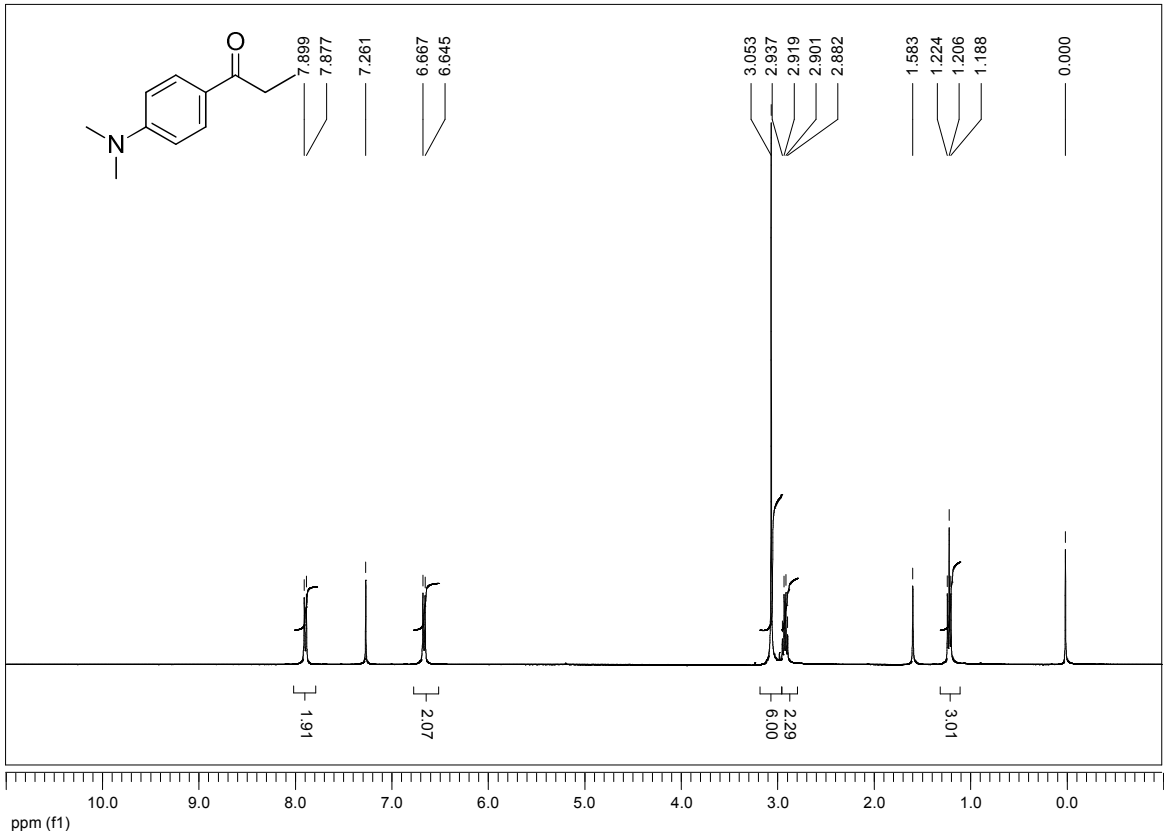
^{1}H NMR of *N*-Methoxy-*N*-methyl-propionamide



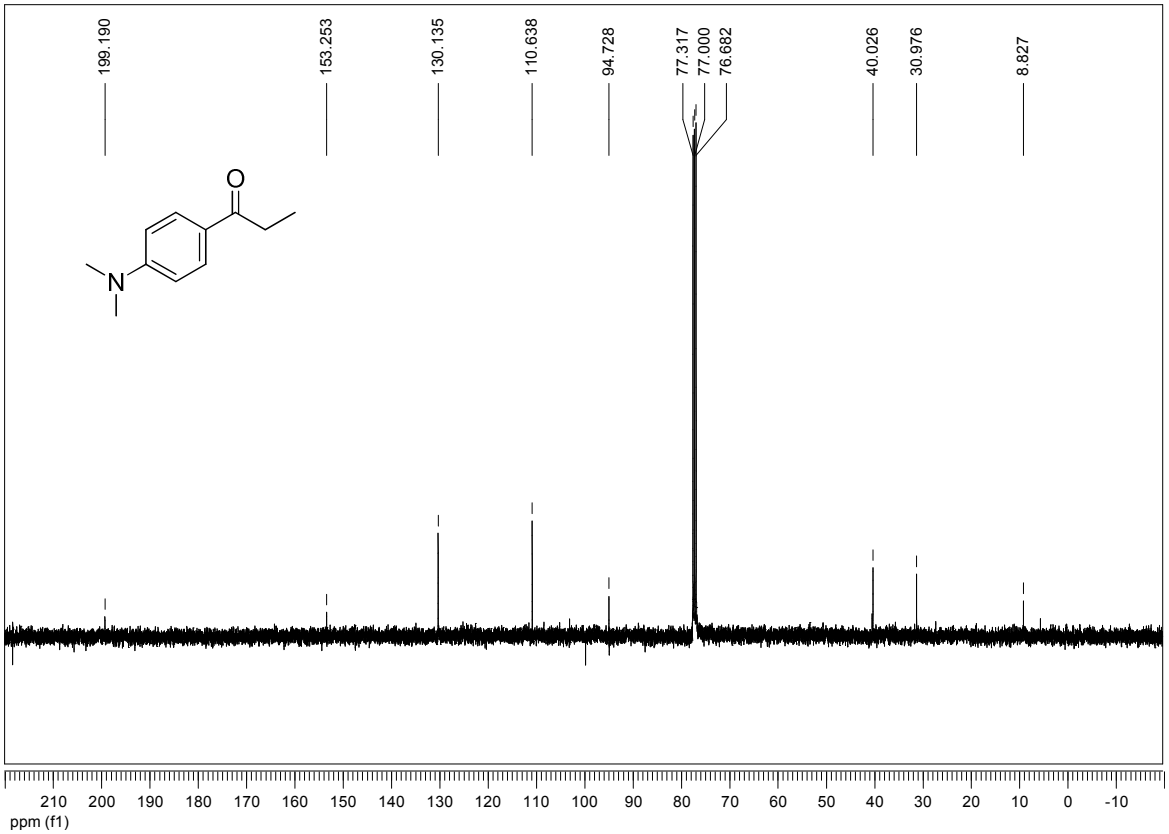
^{13}C NMR of *N*-Methoxy-*N*-methyl-propionamide



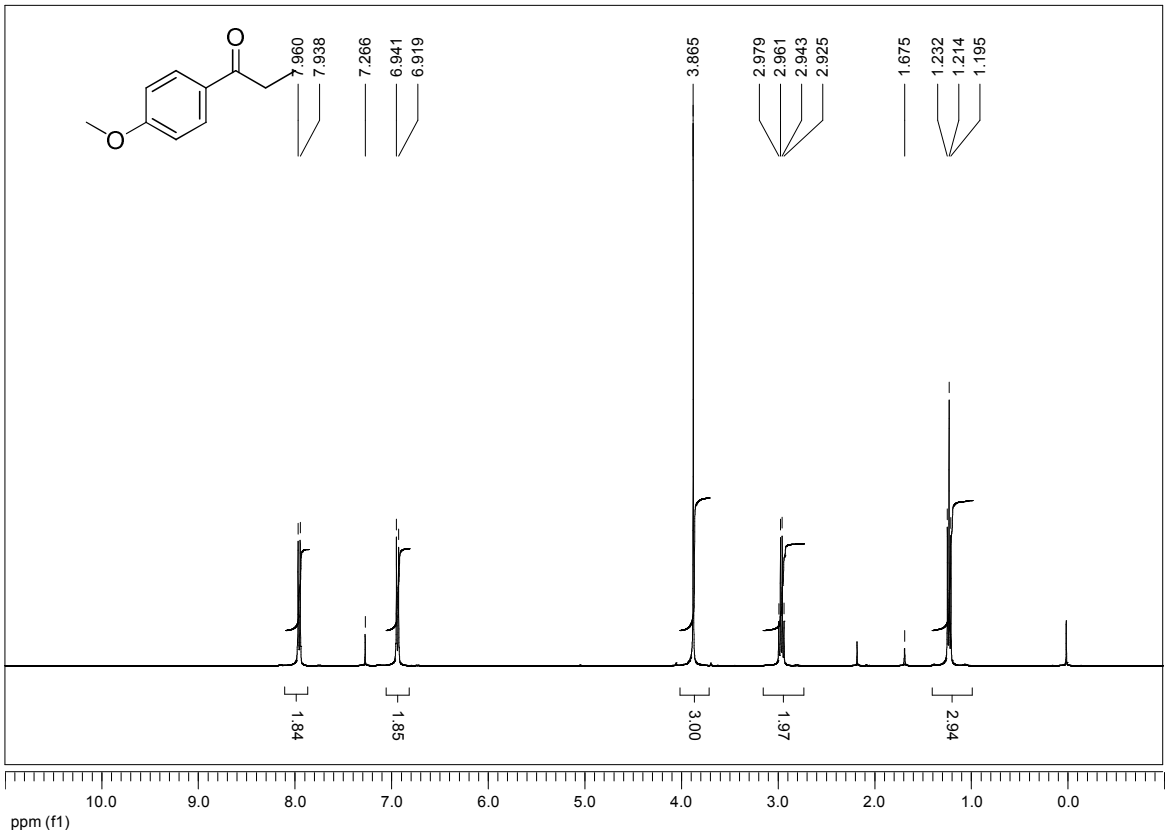
^{1}H NMR of **1b**



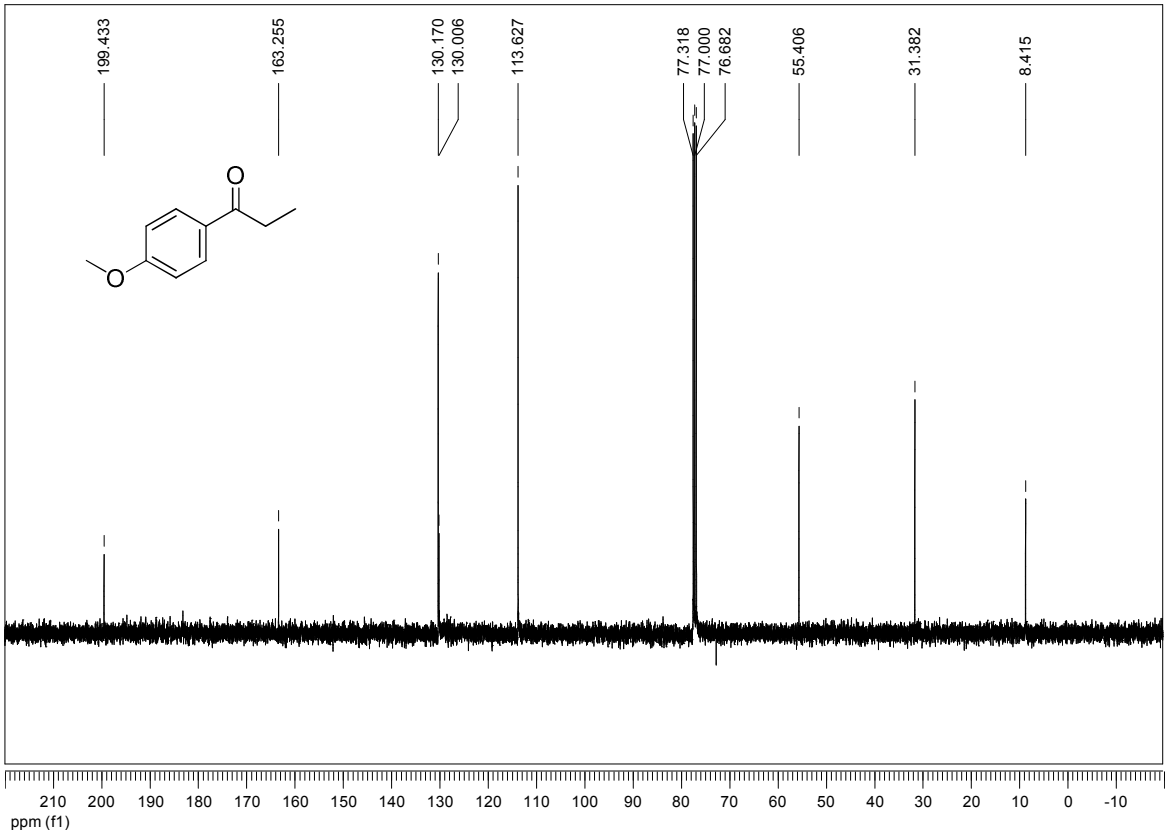
^{13}C NMR of **1b**



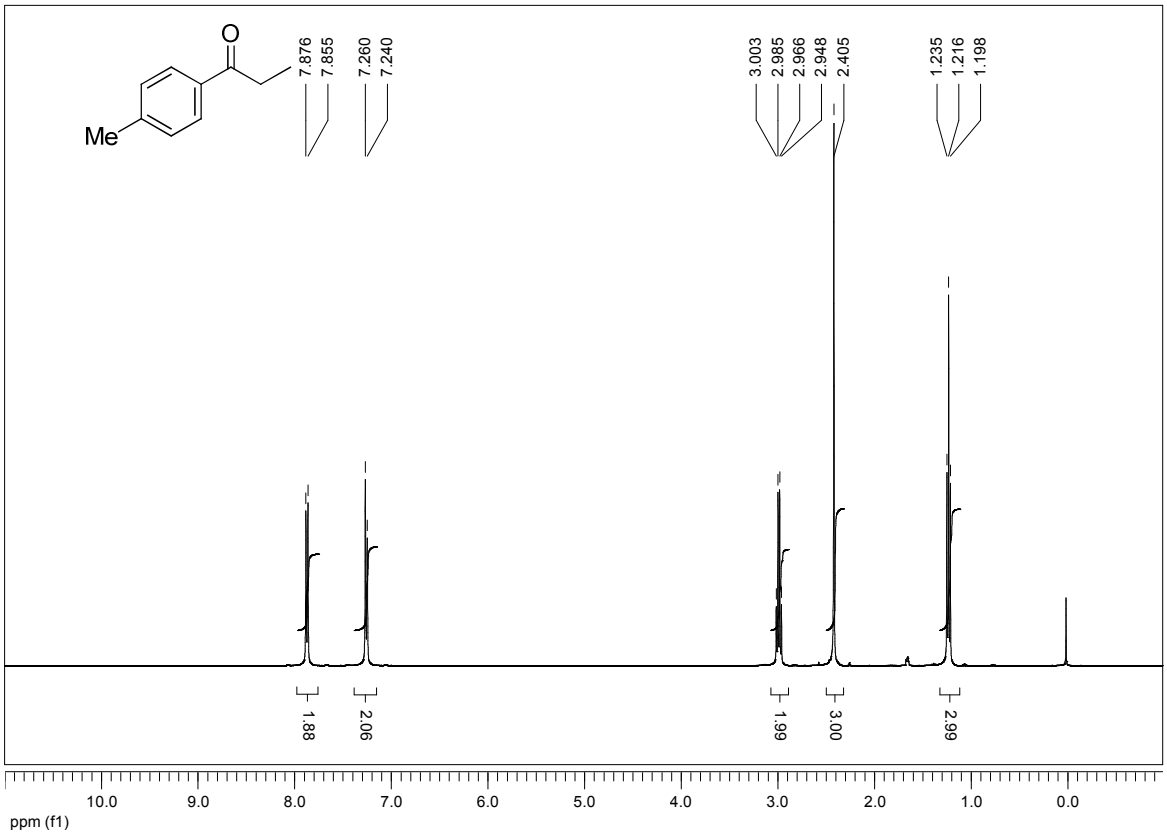
^{1}H NMR of **1c**



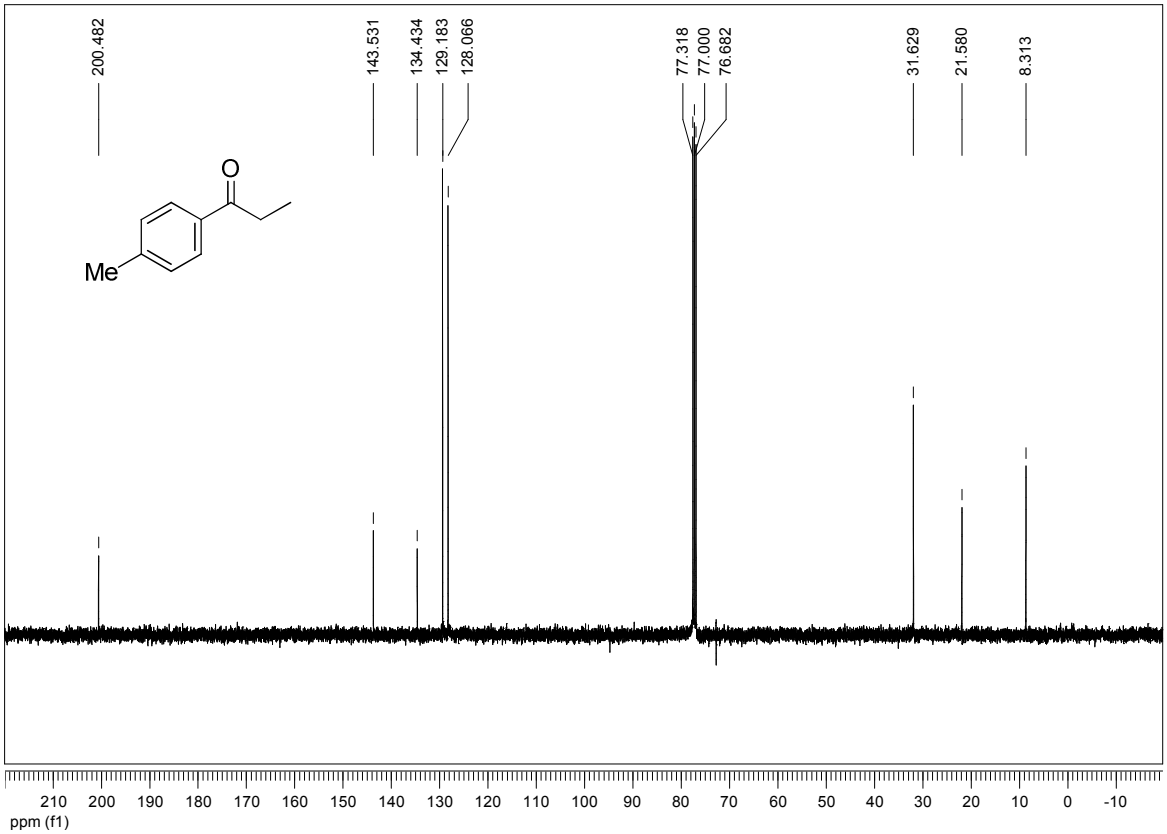
^{13}C NMR of **1c**



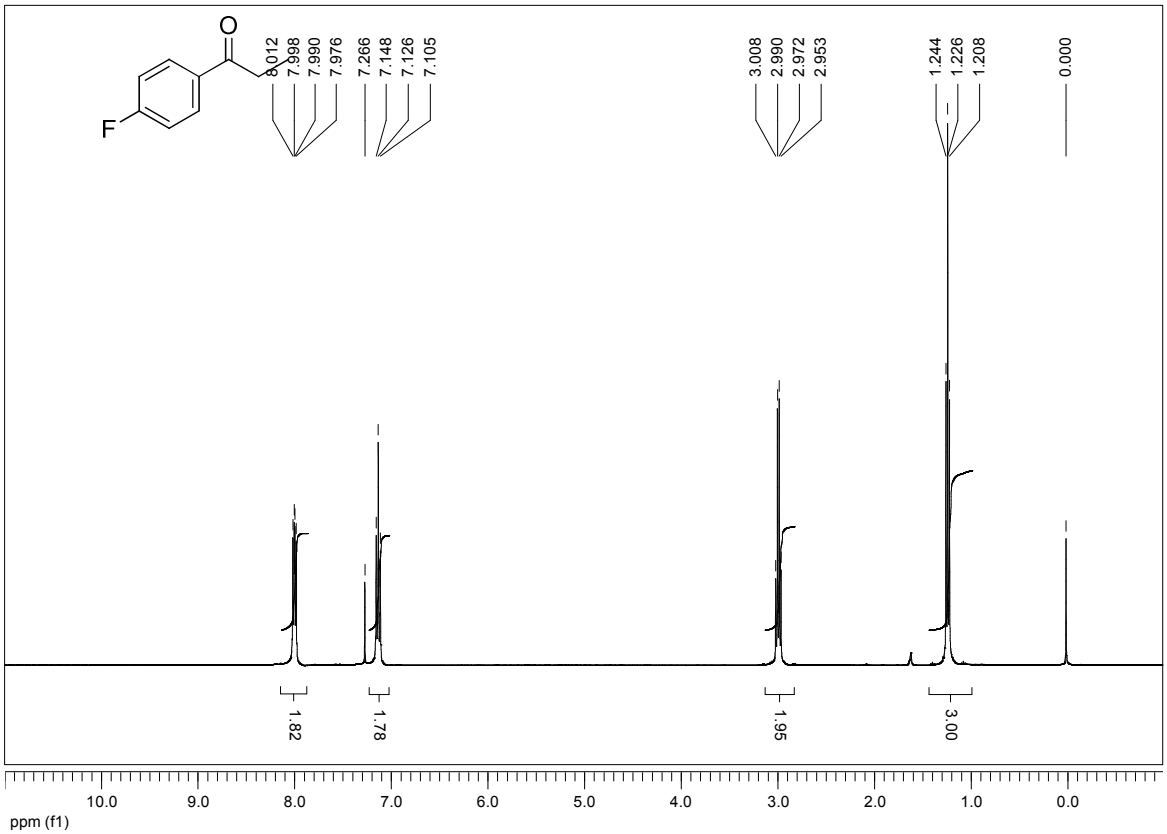
^{1}H NMR of **1d**



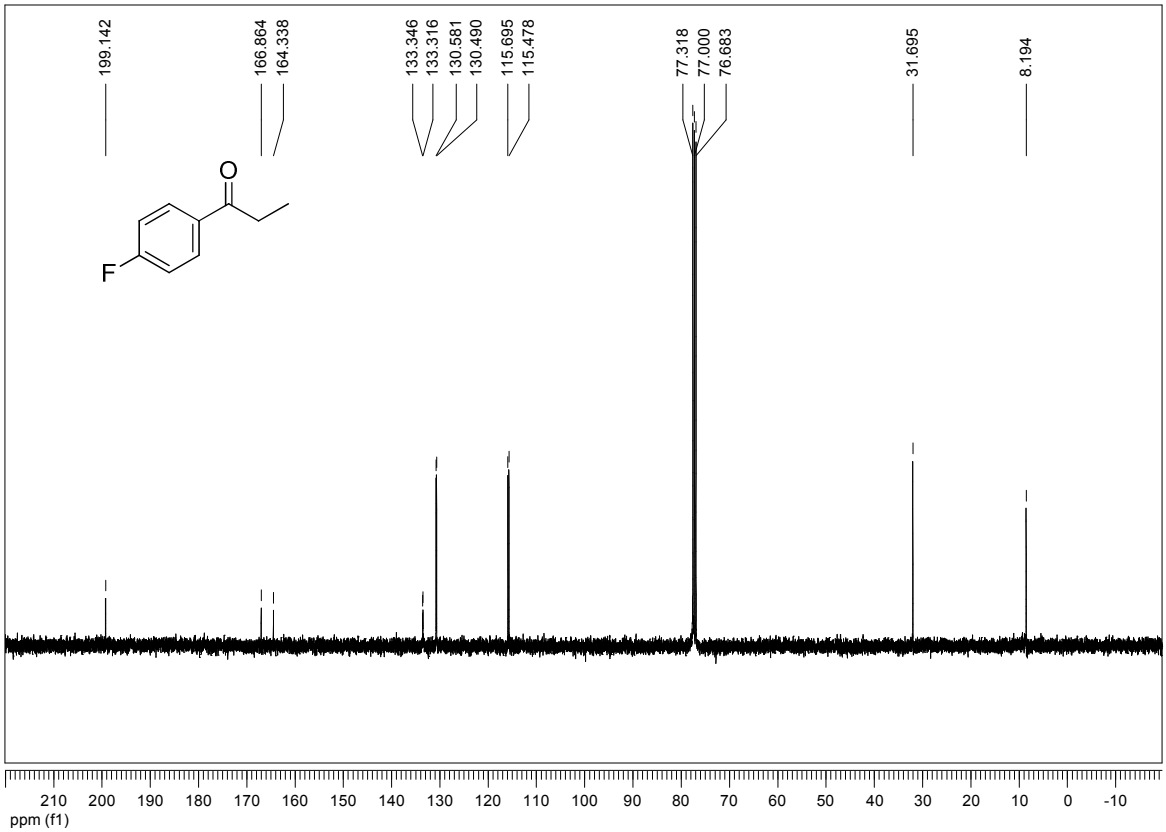
^{13}C NMR of **1d**



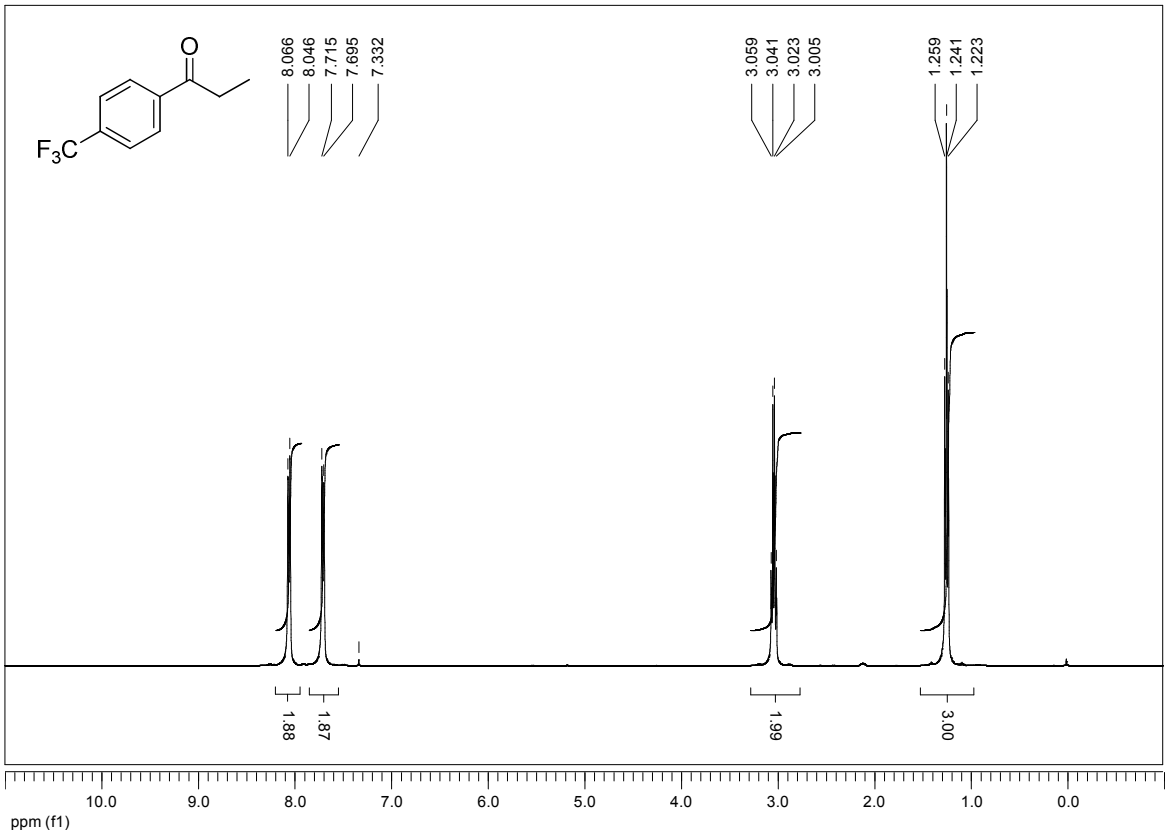
^{1}H NMR of **1e**



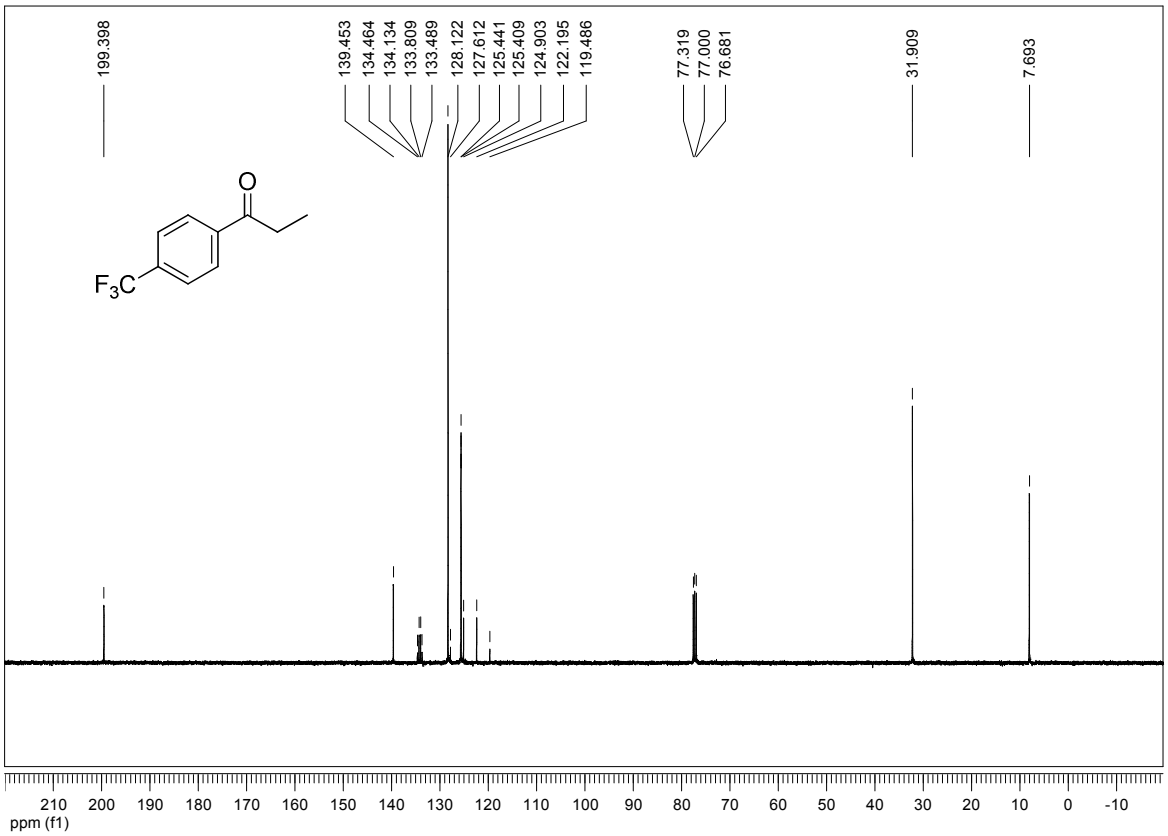
^{13}C NMR of **1e**



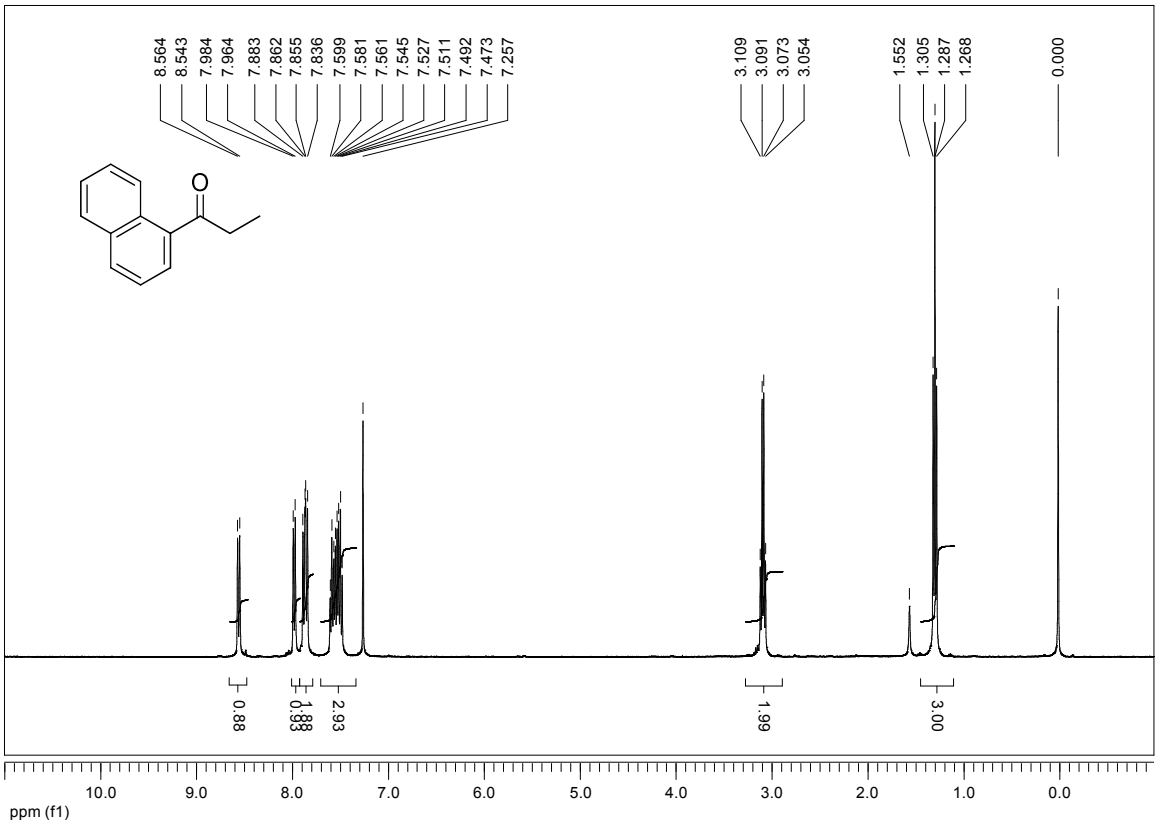
^{1}H NMR of **1f**



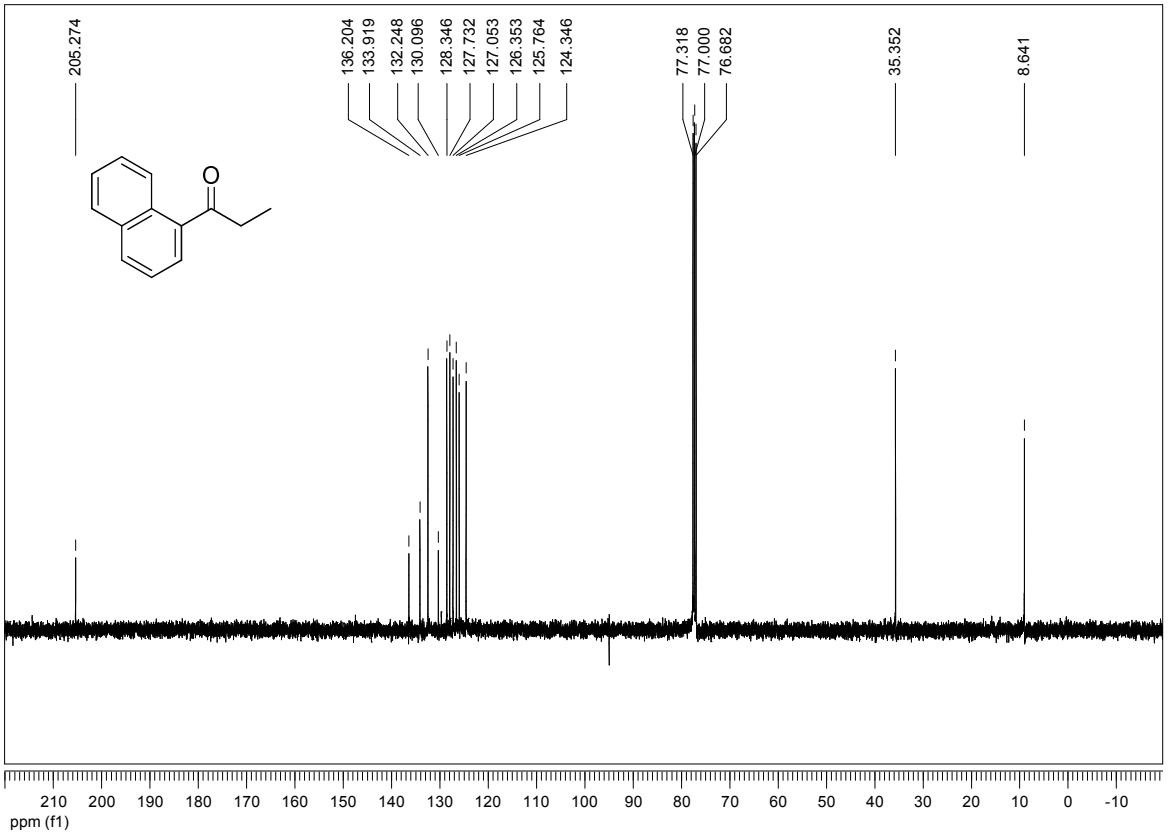
^{13}C NMR of **1f**



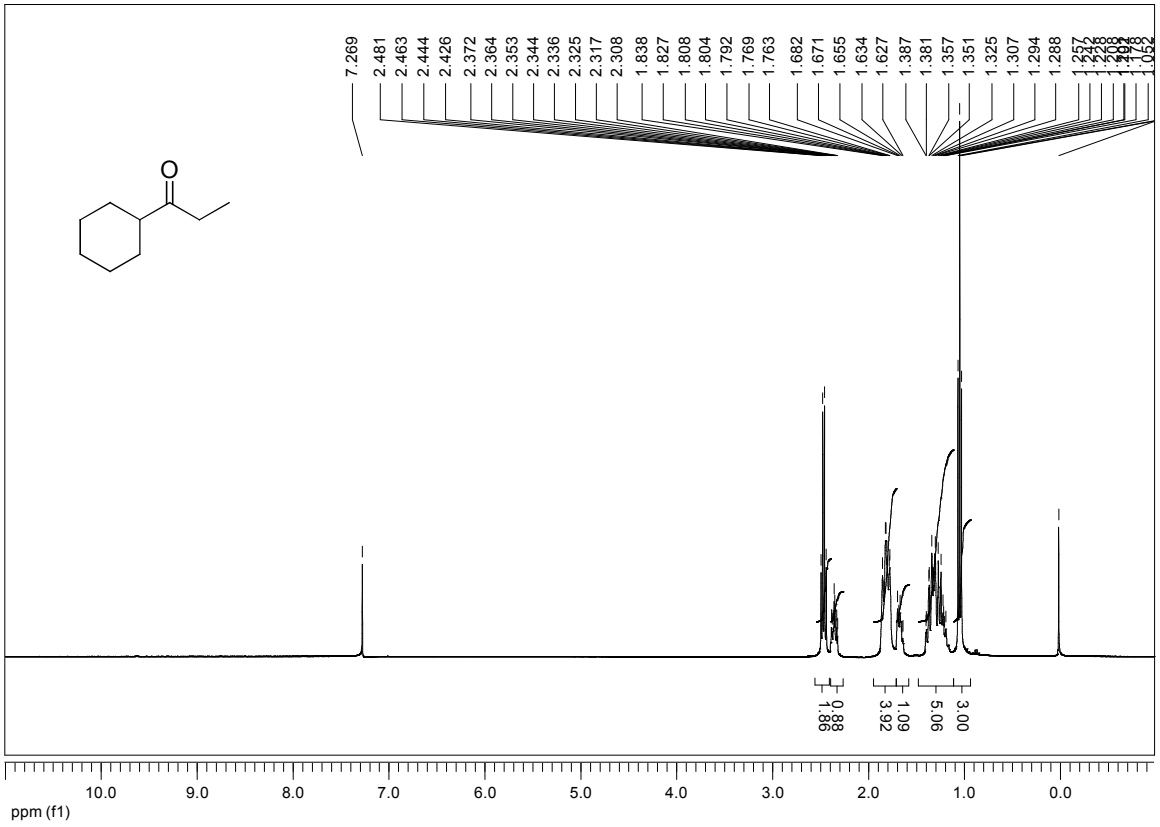
^{1}H NMR of **1g**



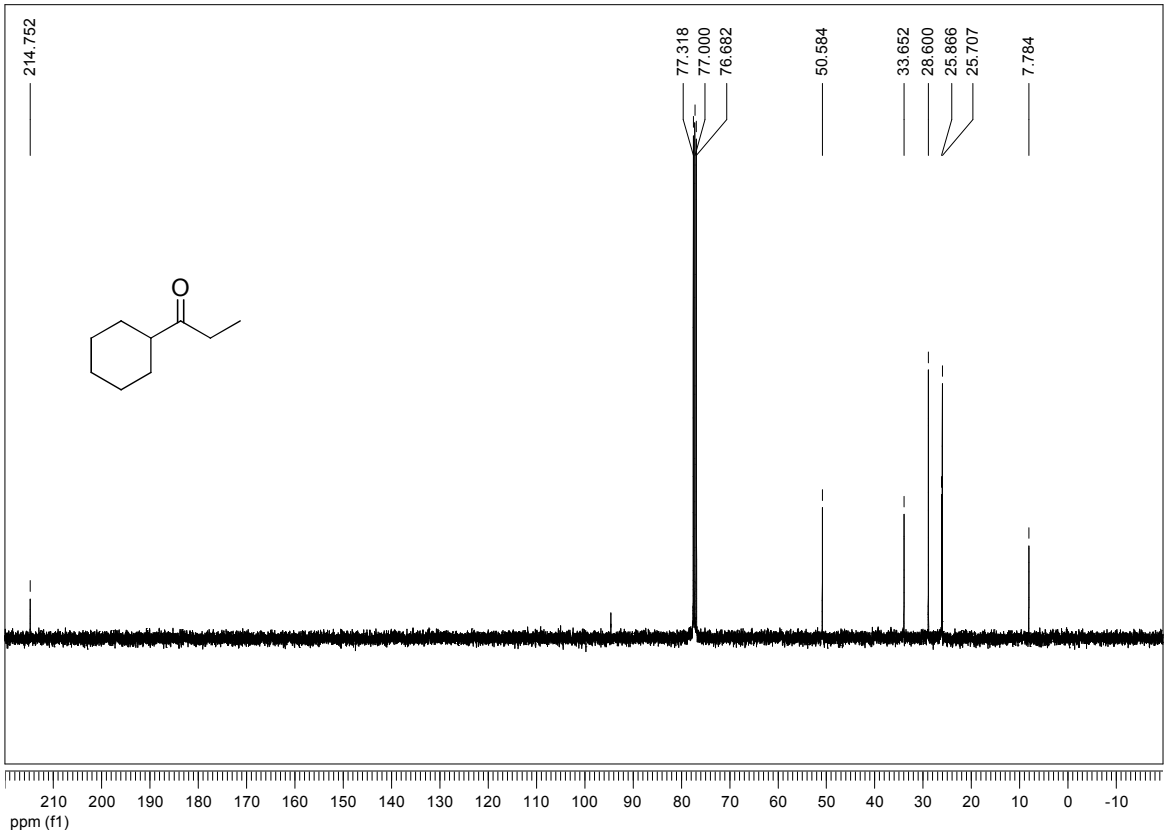
^{13}C NMR of **1g**



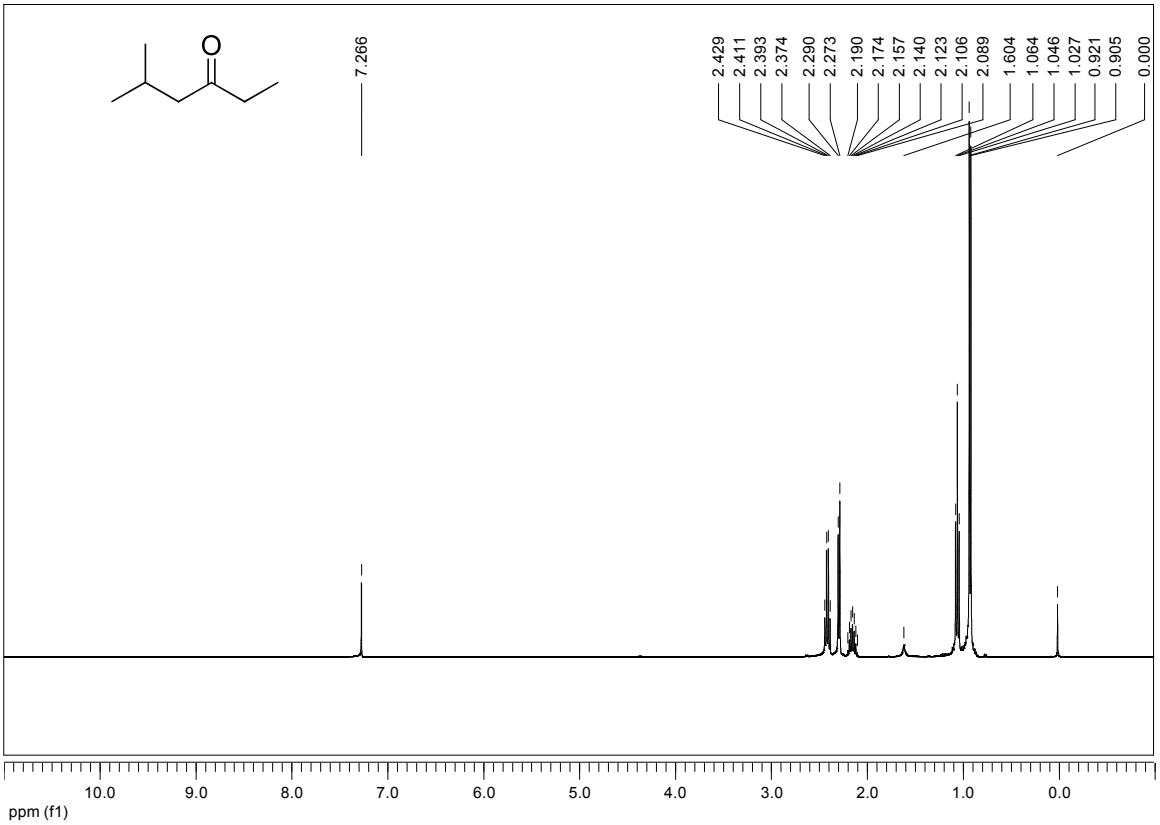
^{1}H NMR of **1h**



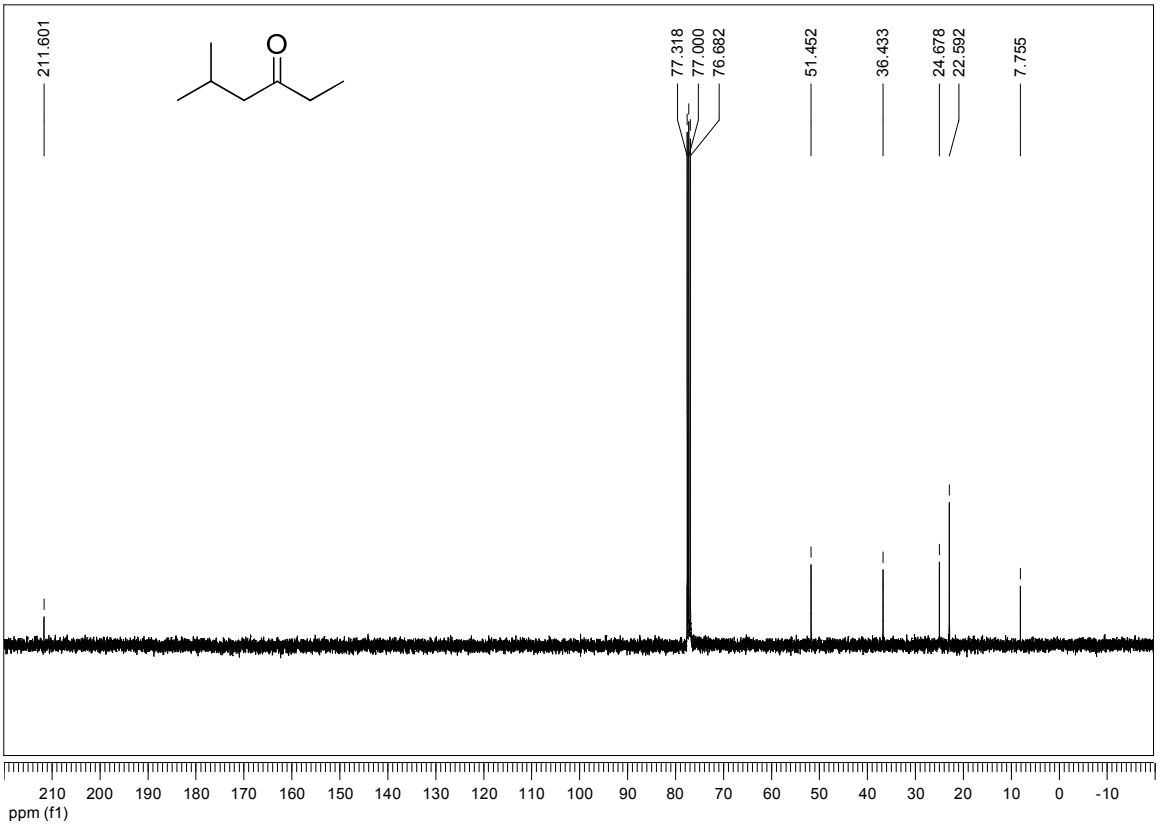
^{13}C NMR of **1h**



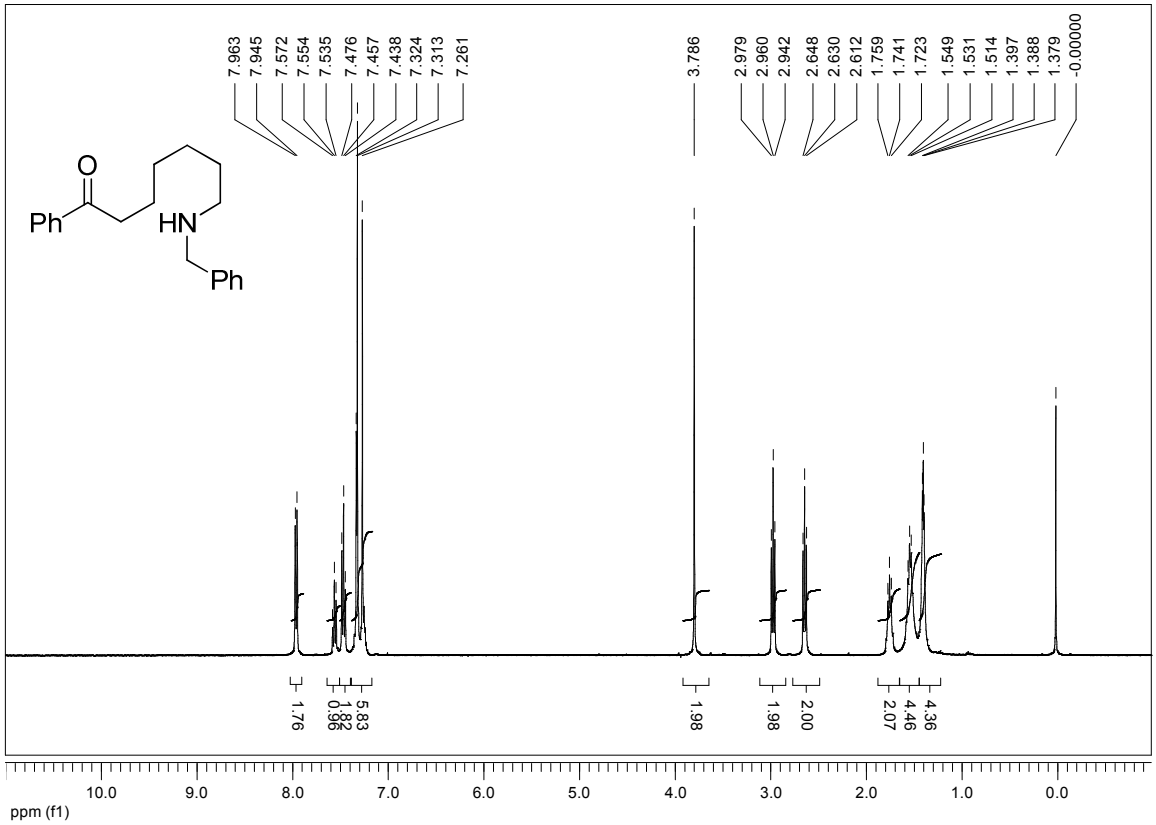
^{1}H NMR of **1i**



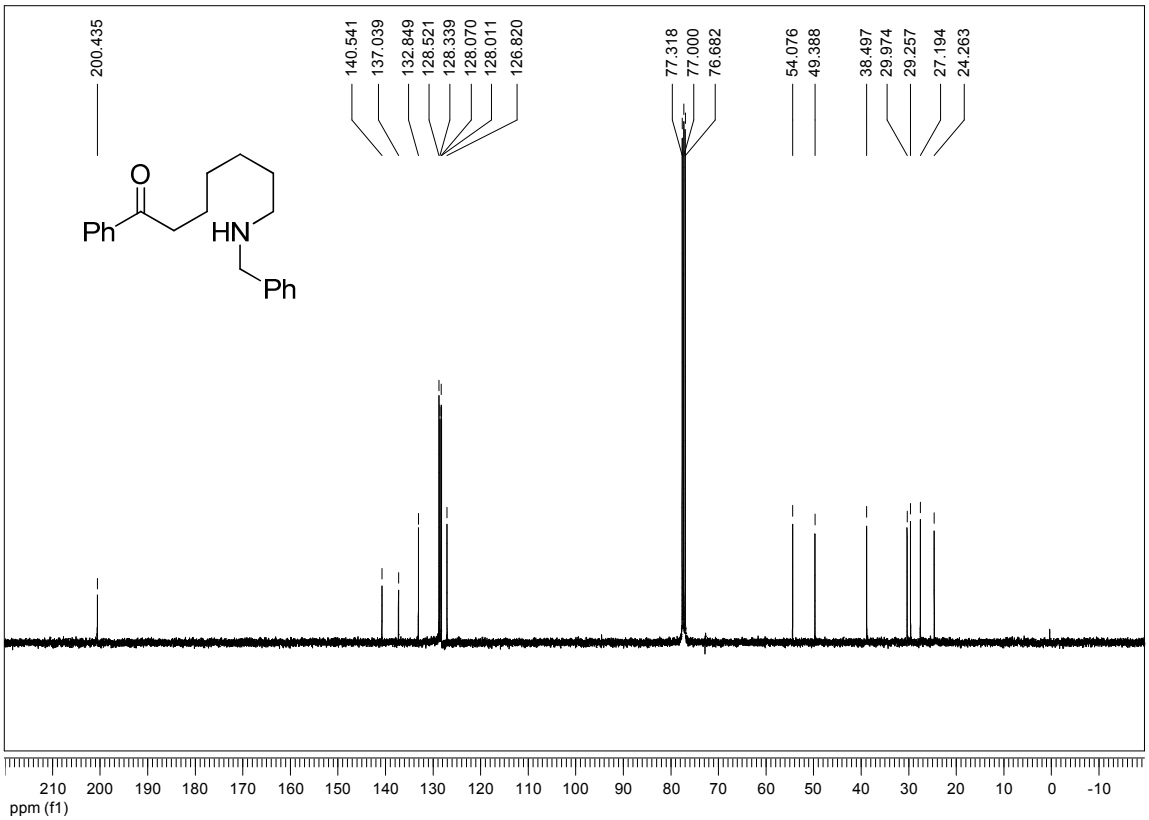
^{13}C NMR of **1i**



^{1}H NMR of **4**

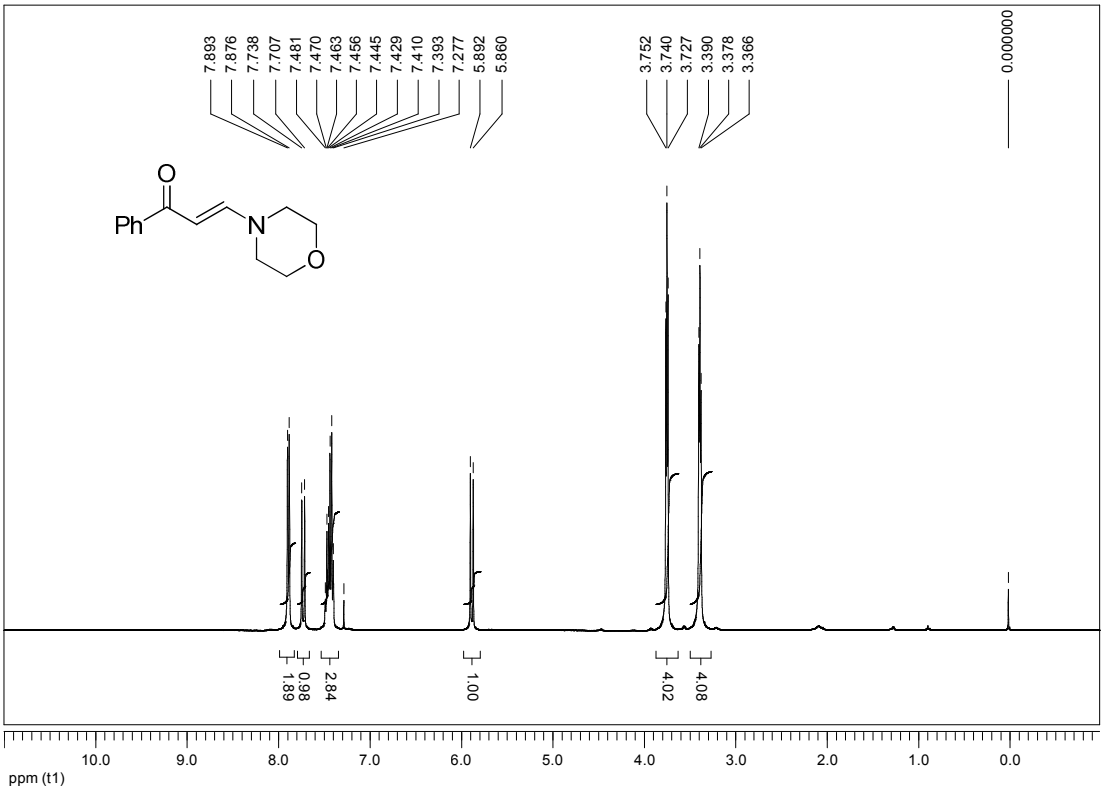


^{13}C NMR of **4**

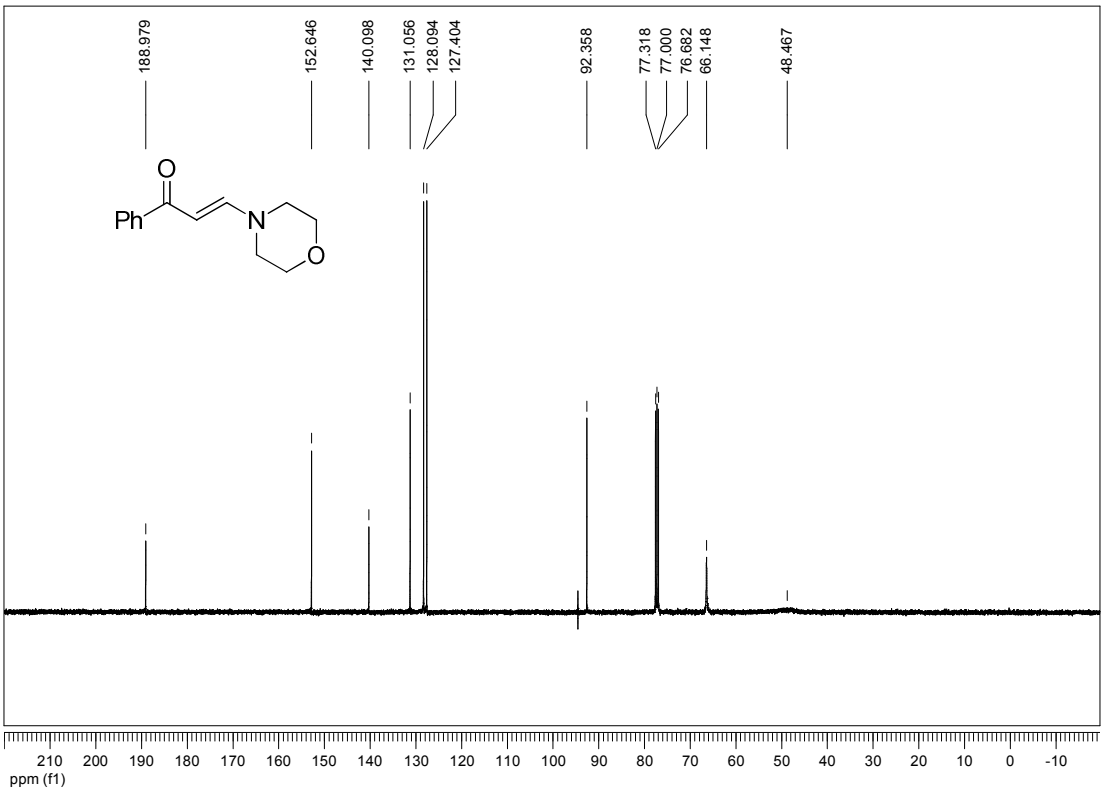


X. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of Products 3 and 5.

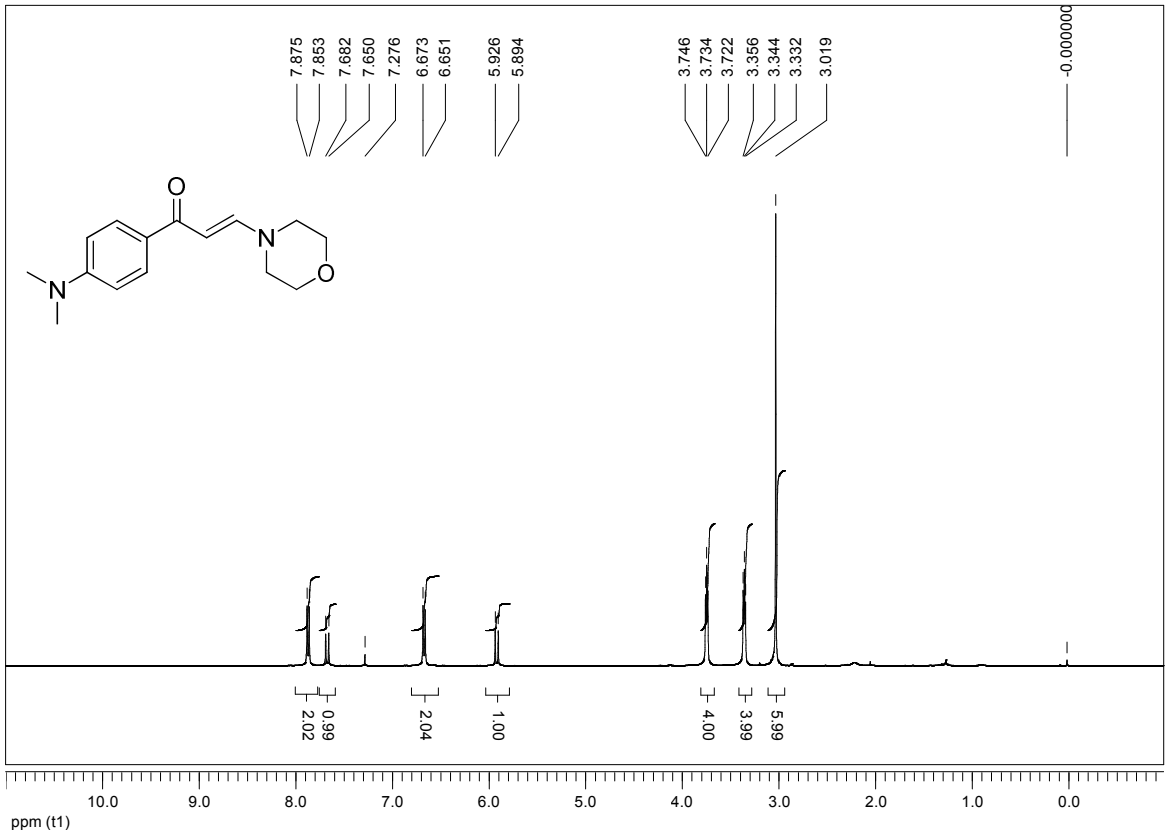
^{1}H NMR of **3a**



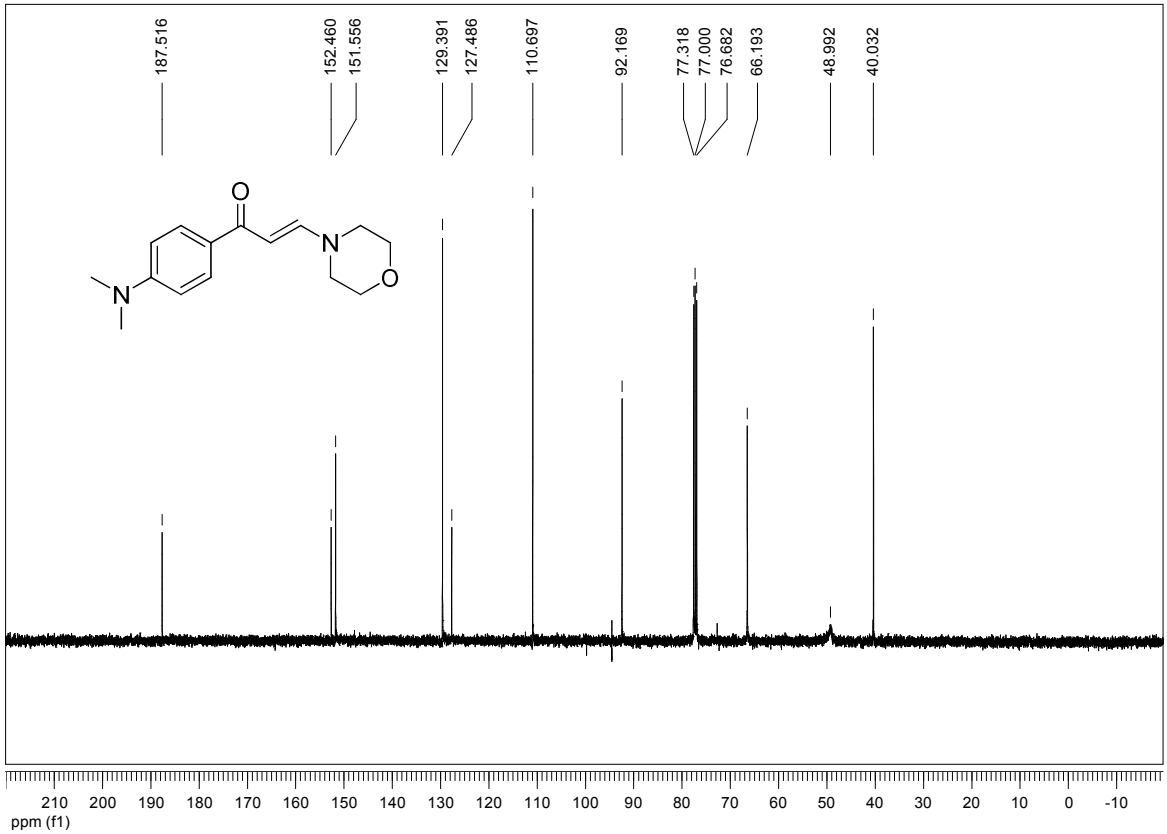
^{13}C NMR of **3a**



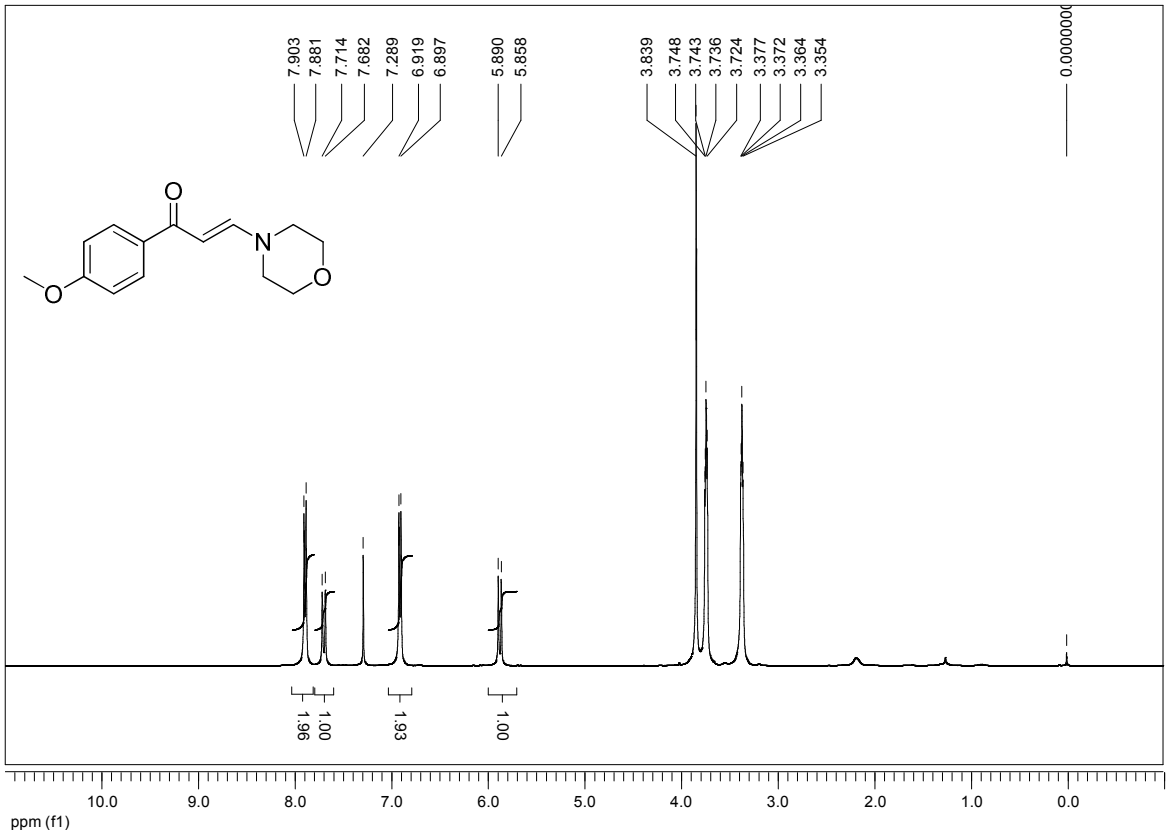
^{1}H NMR of **3b**



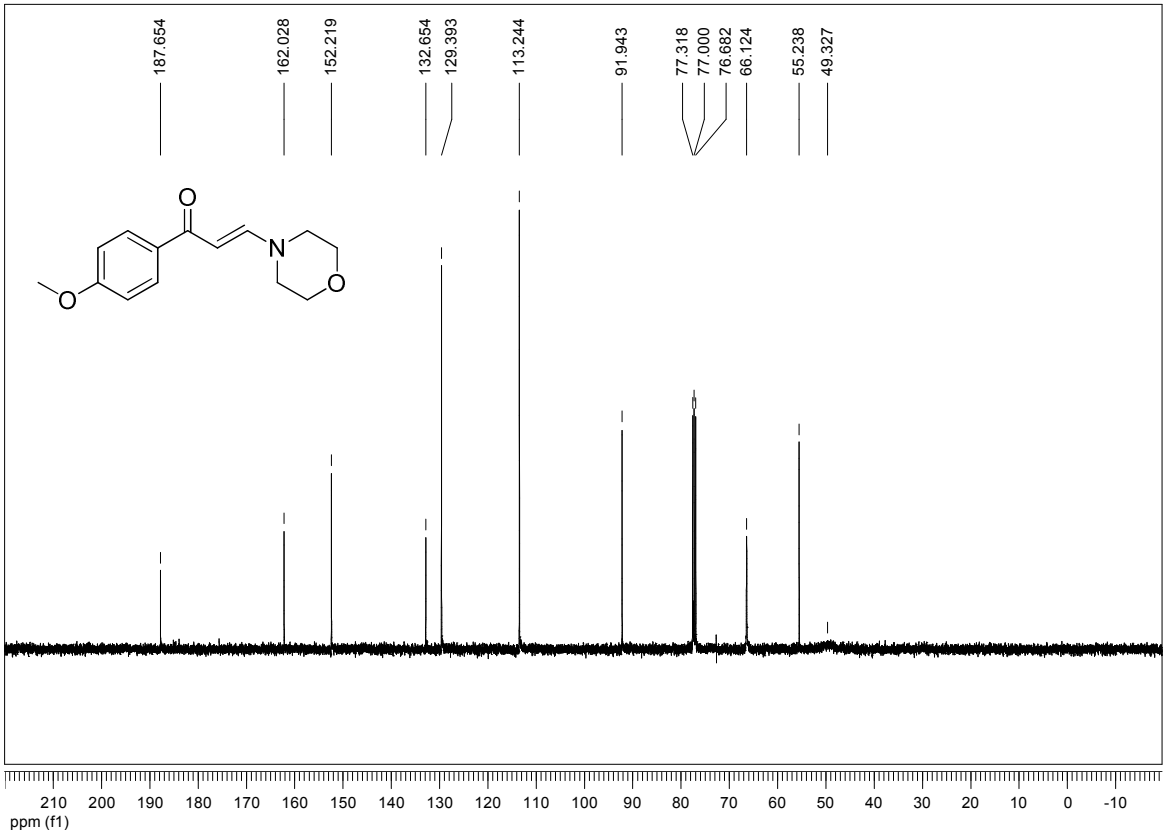
^{13}C NMR of **3b**



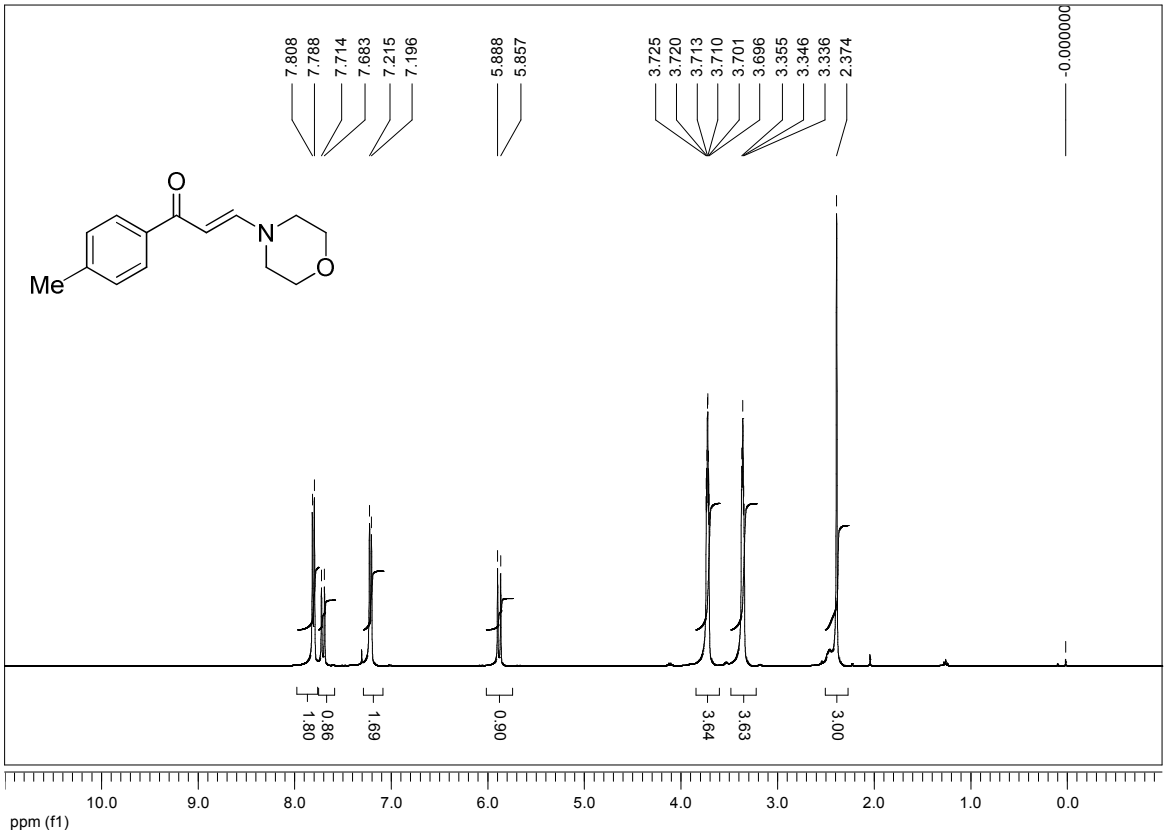
^{1}H NMR of **3c**



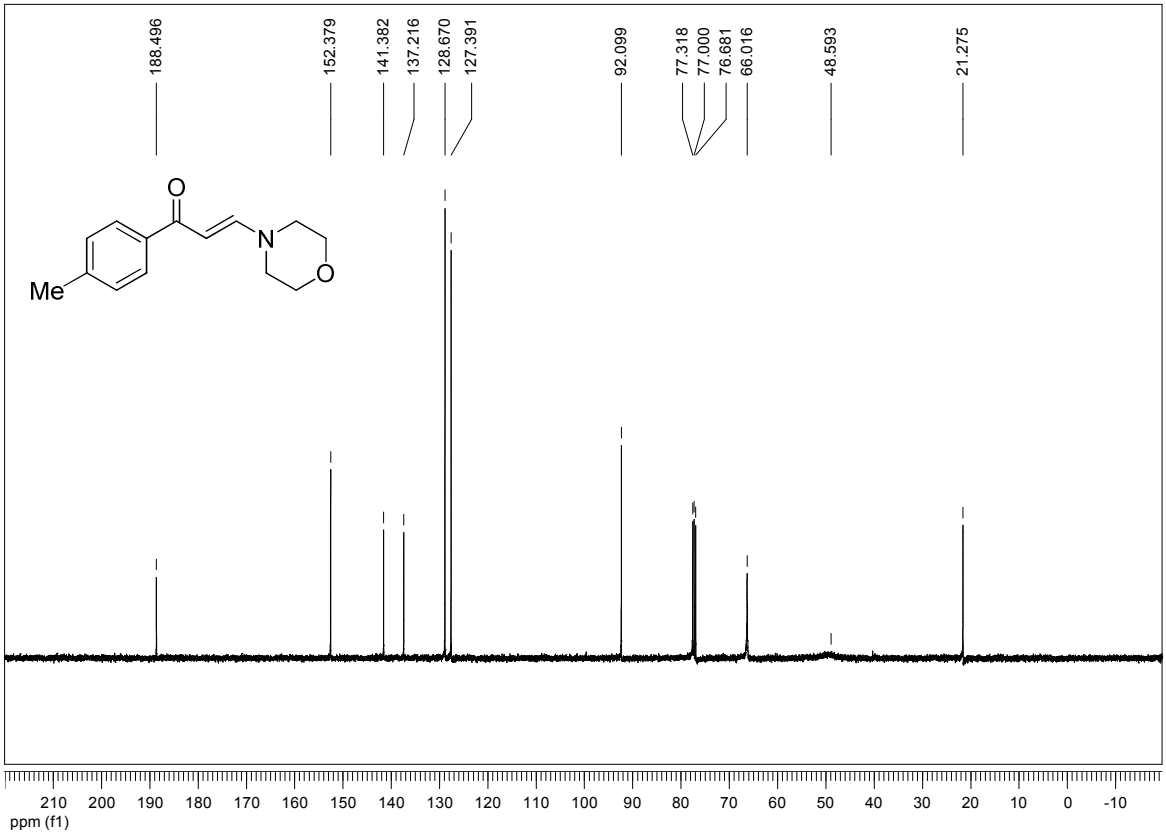
^{13}C NMR of **3c**



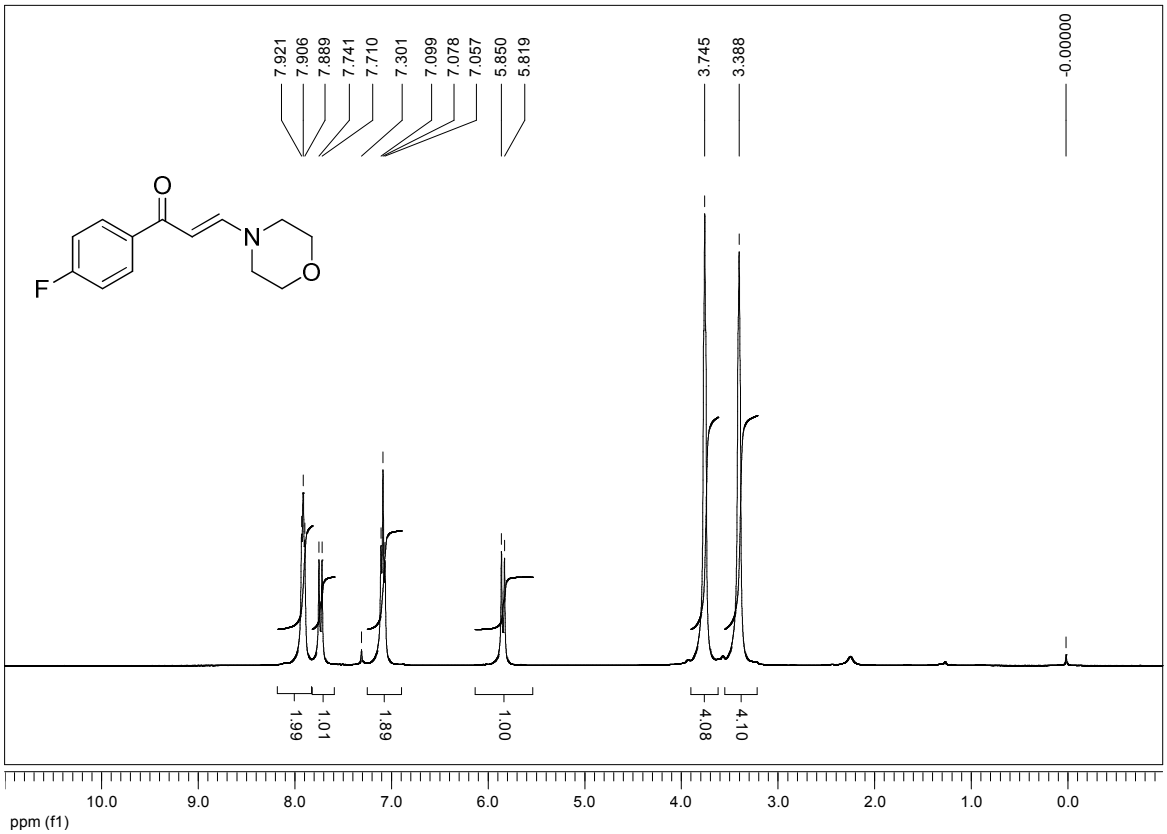
^{1}H NMR of **3d**



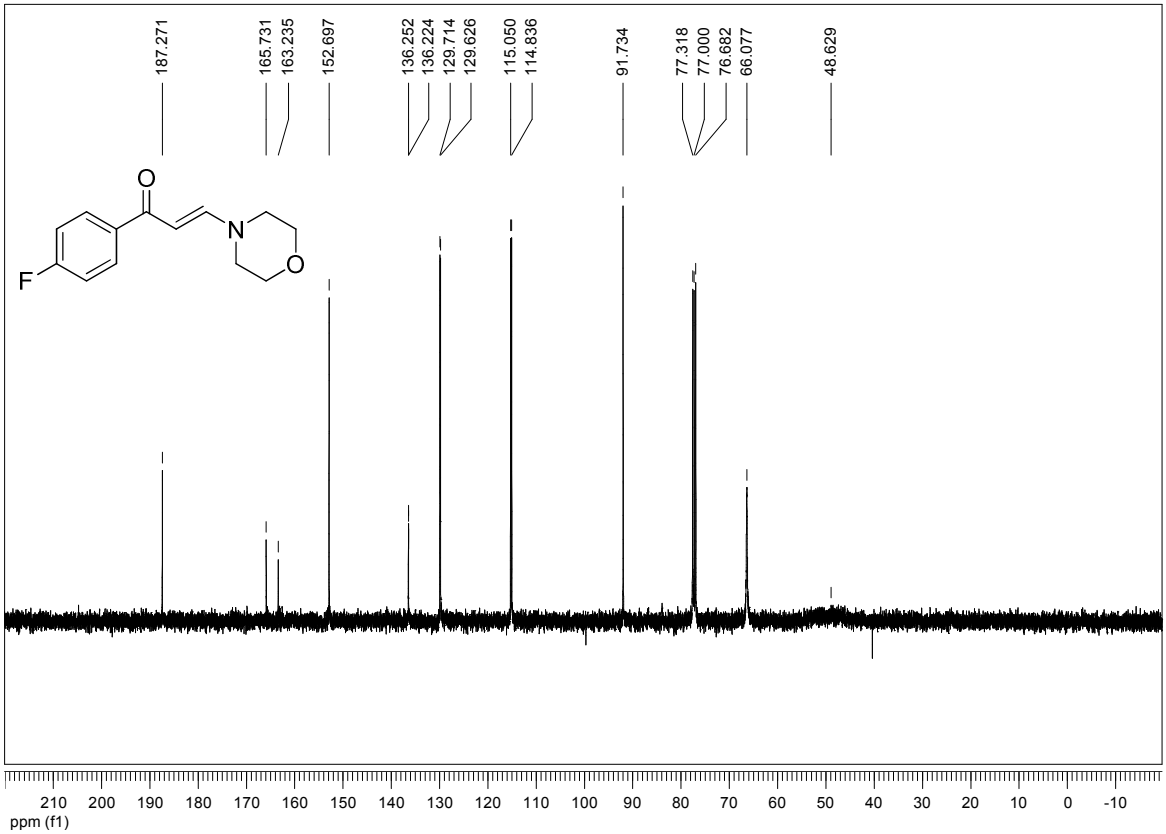
^{13}C NMR of **3d**



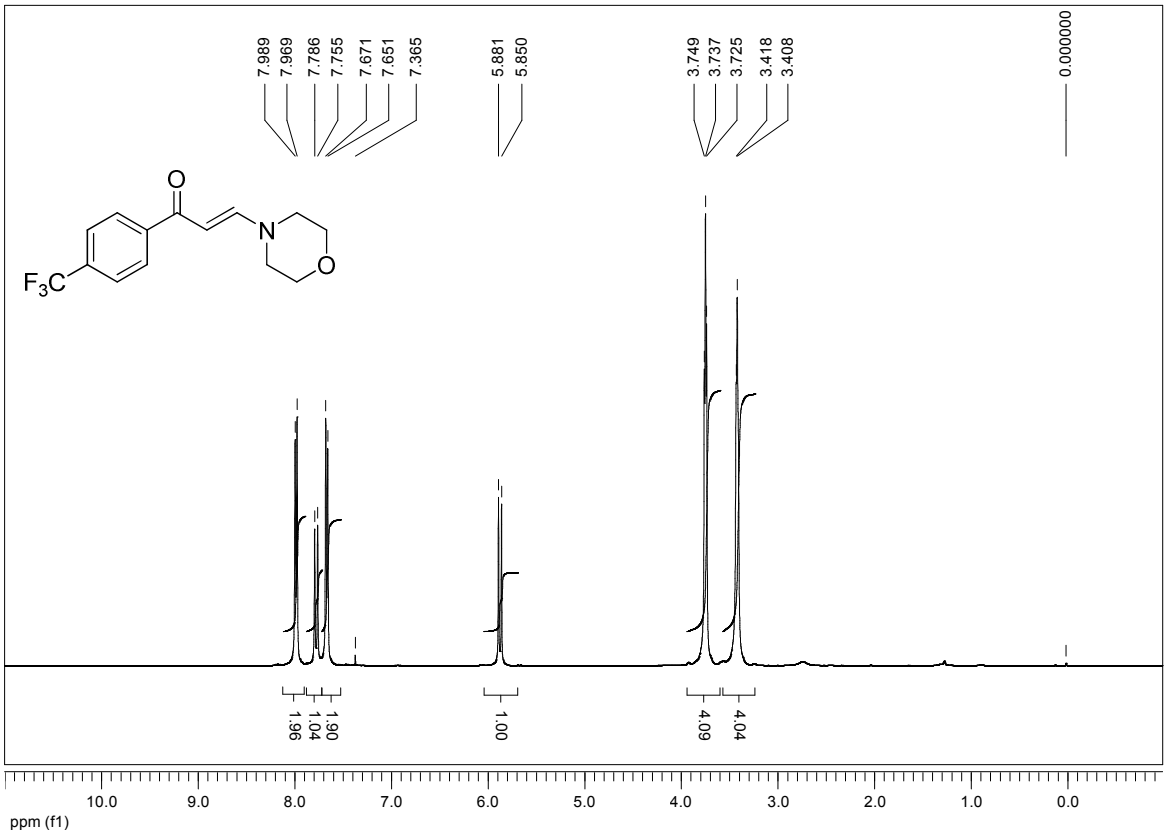
^{1}H NMR of **3e**



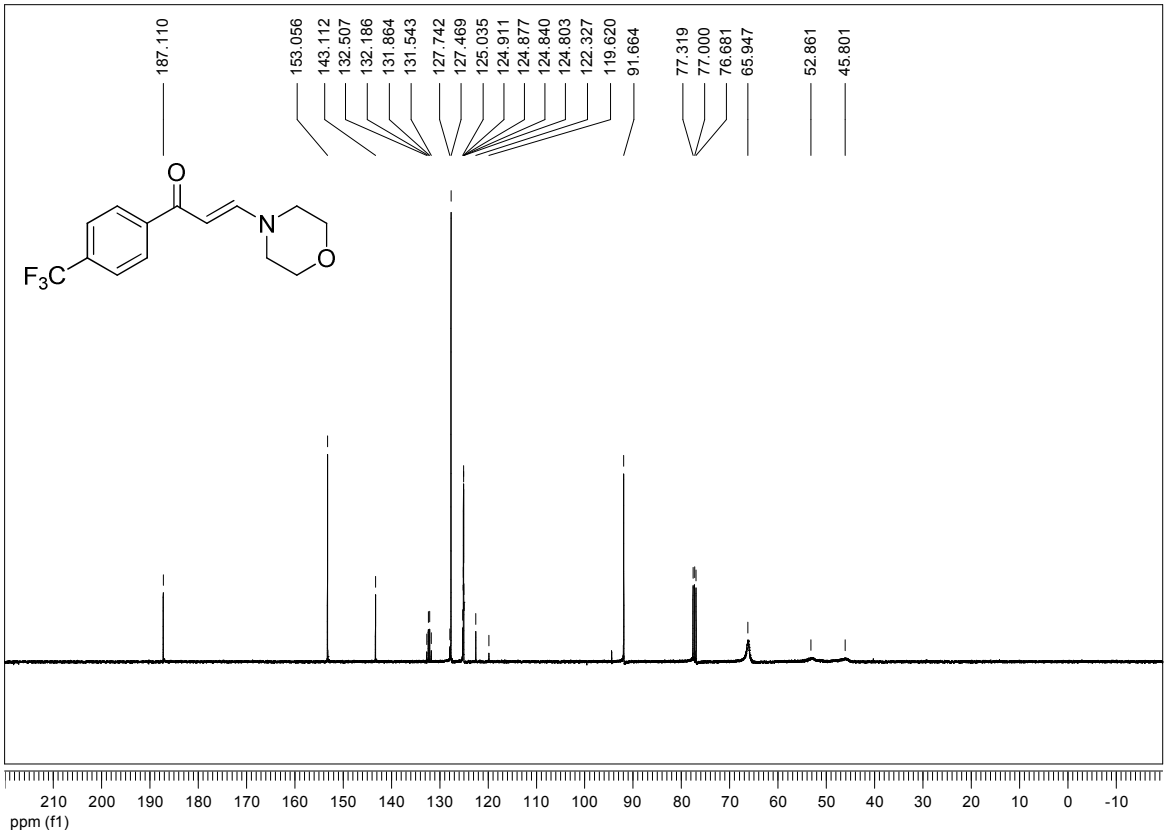
^{13}C NMR of **3e**



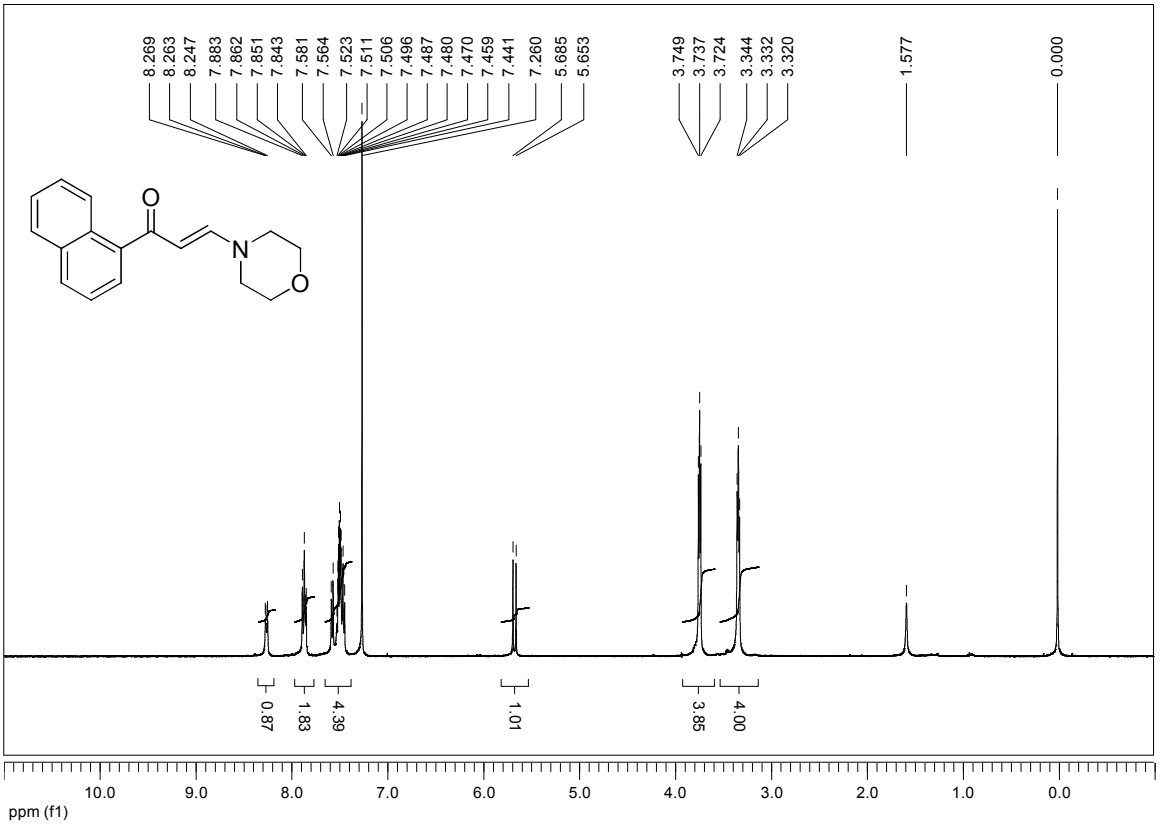
^{1}H NMR of **3f**



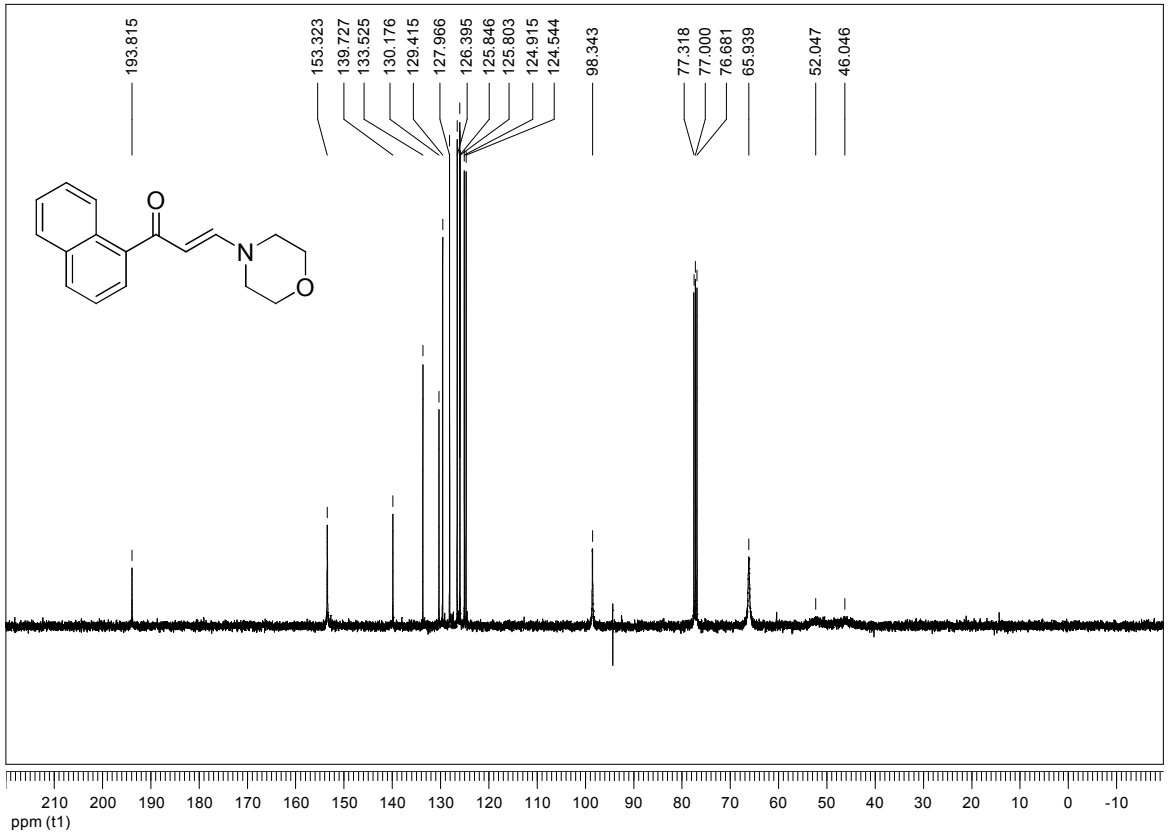
^{13}C NMR of **3f**



^{1}H NMR of **3g**



^{13}C NMR of **3g**



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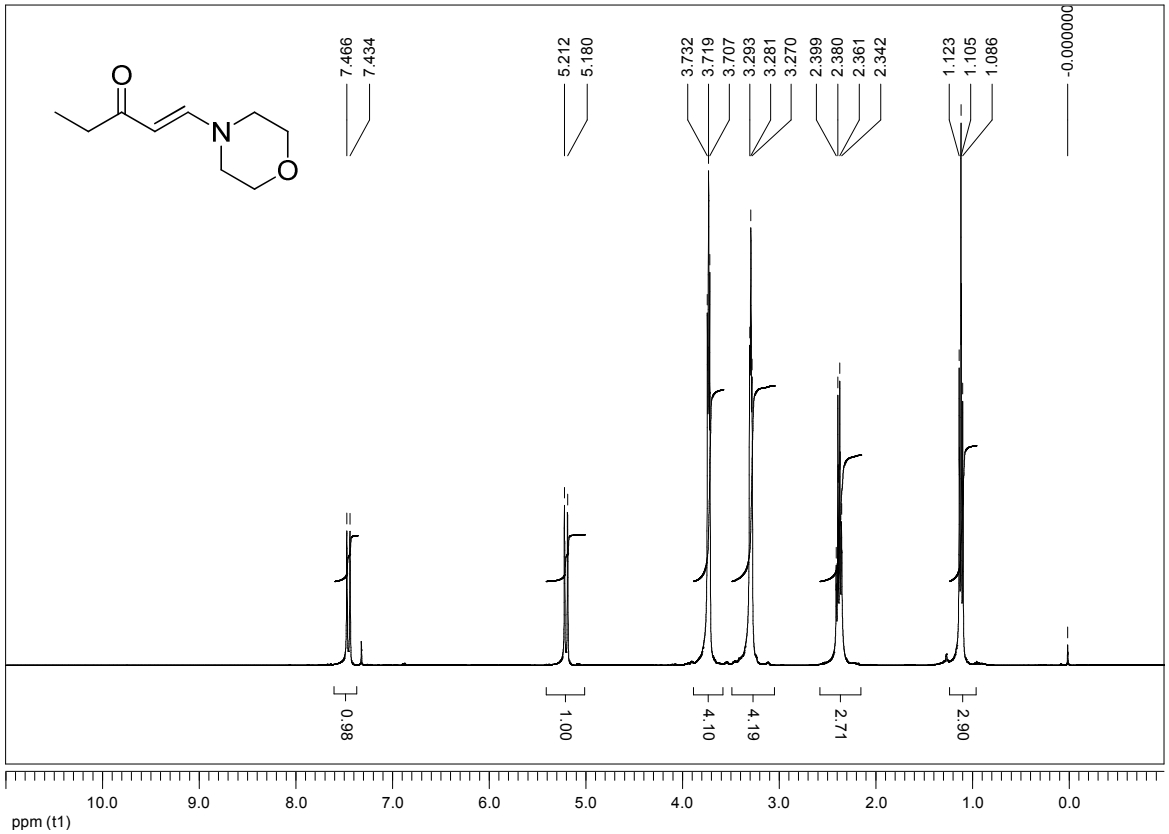

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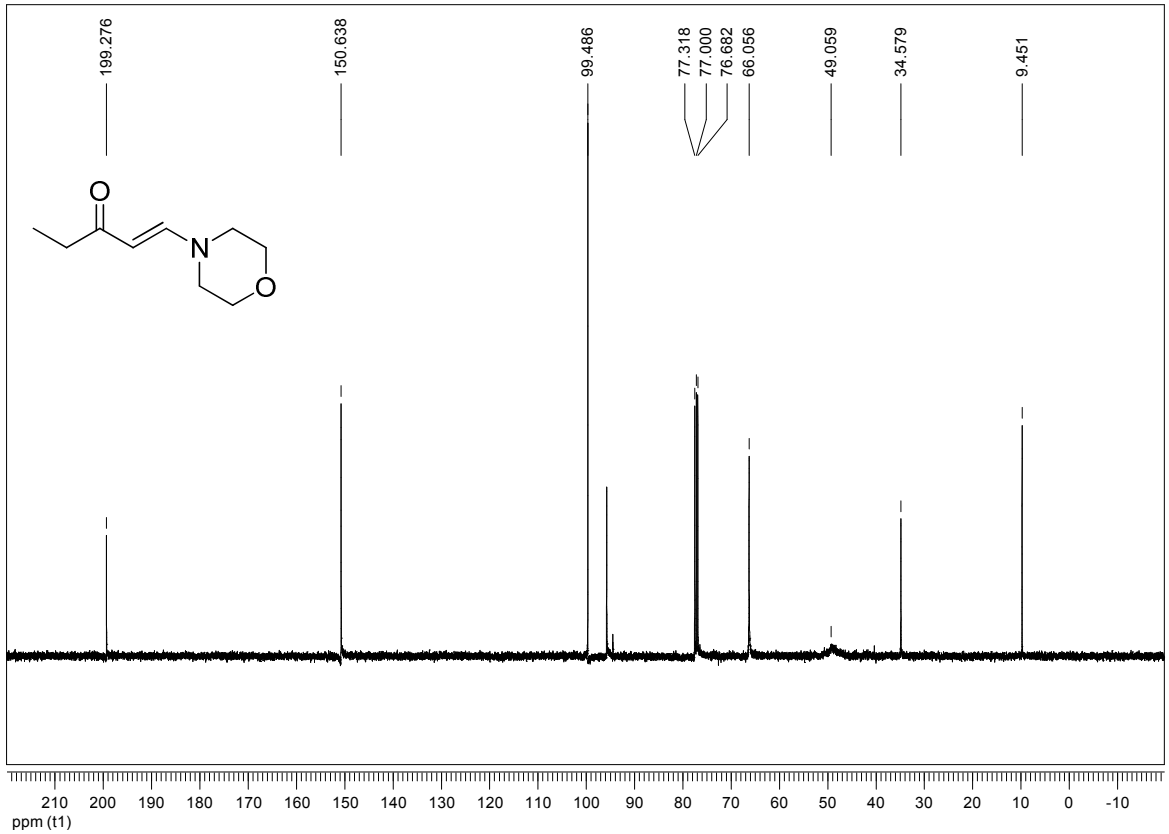
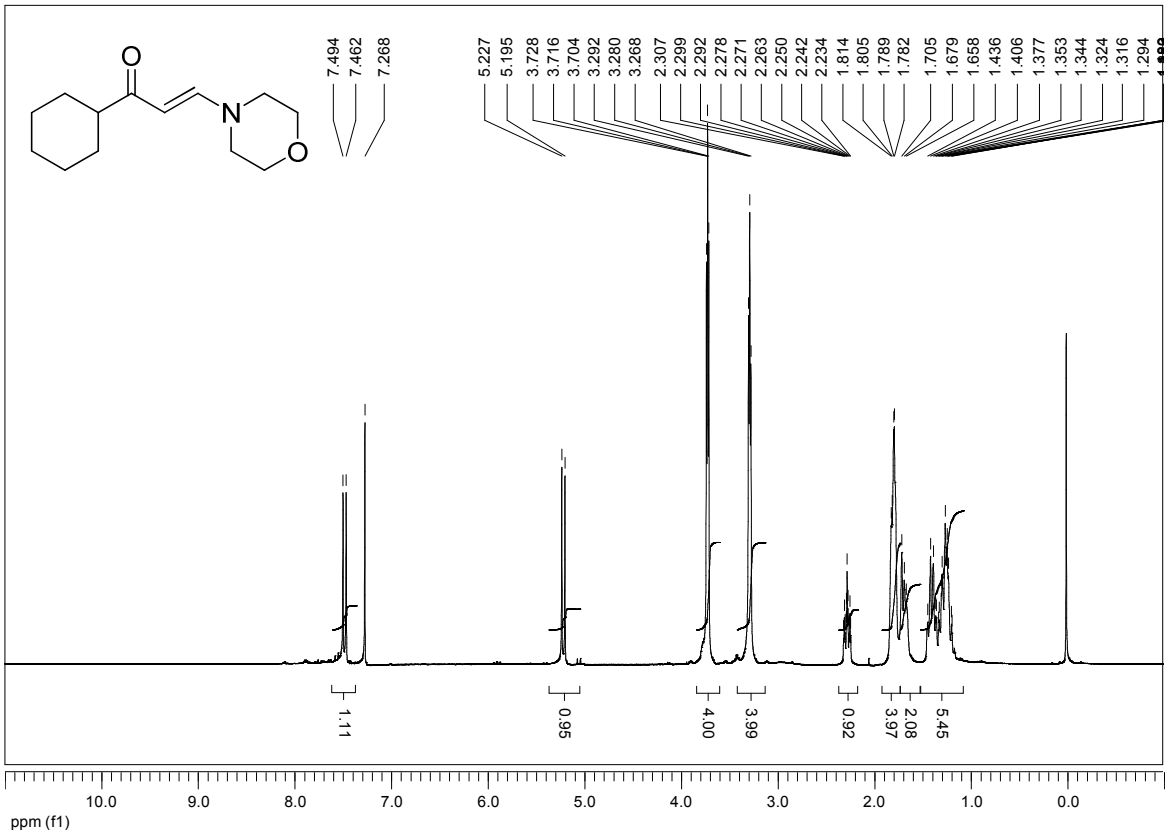
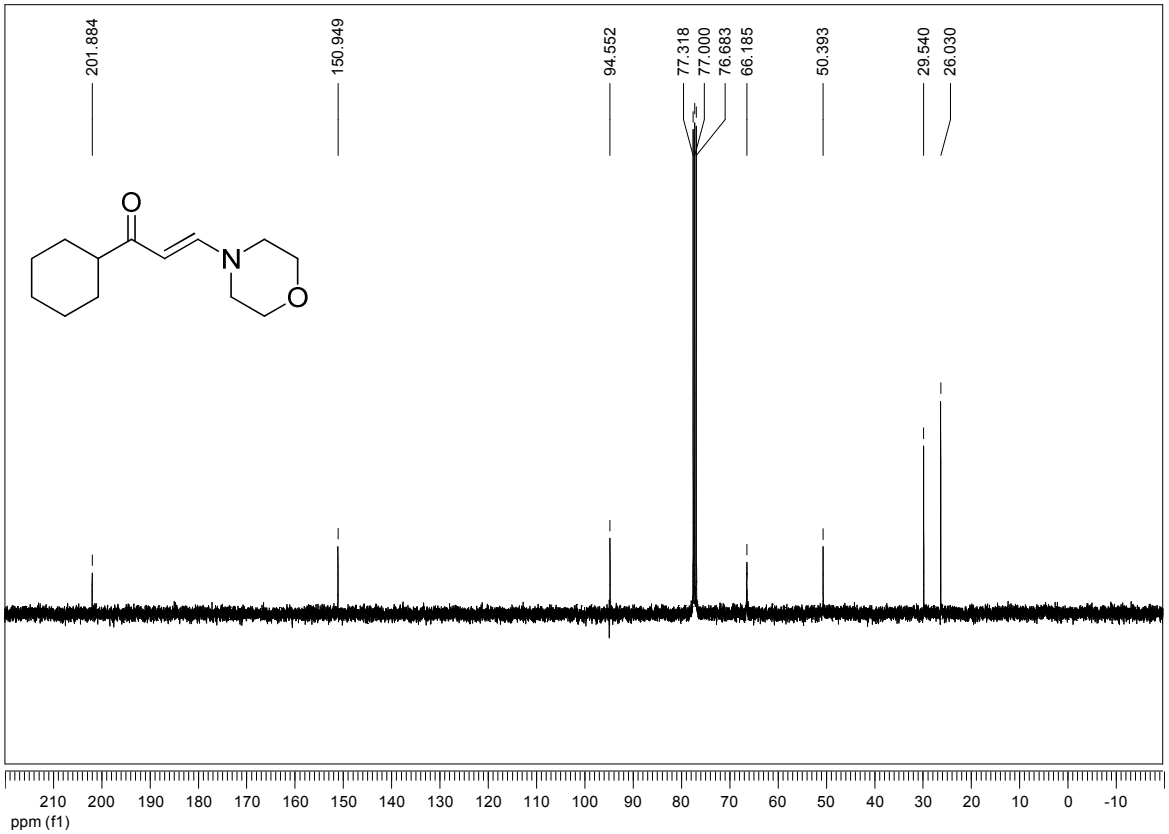


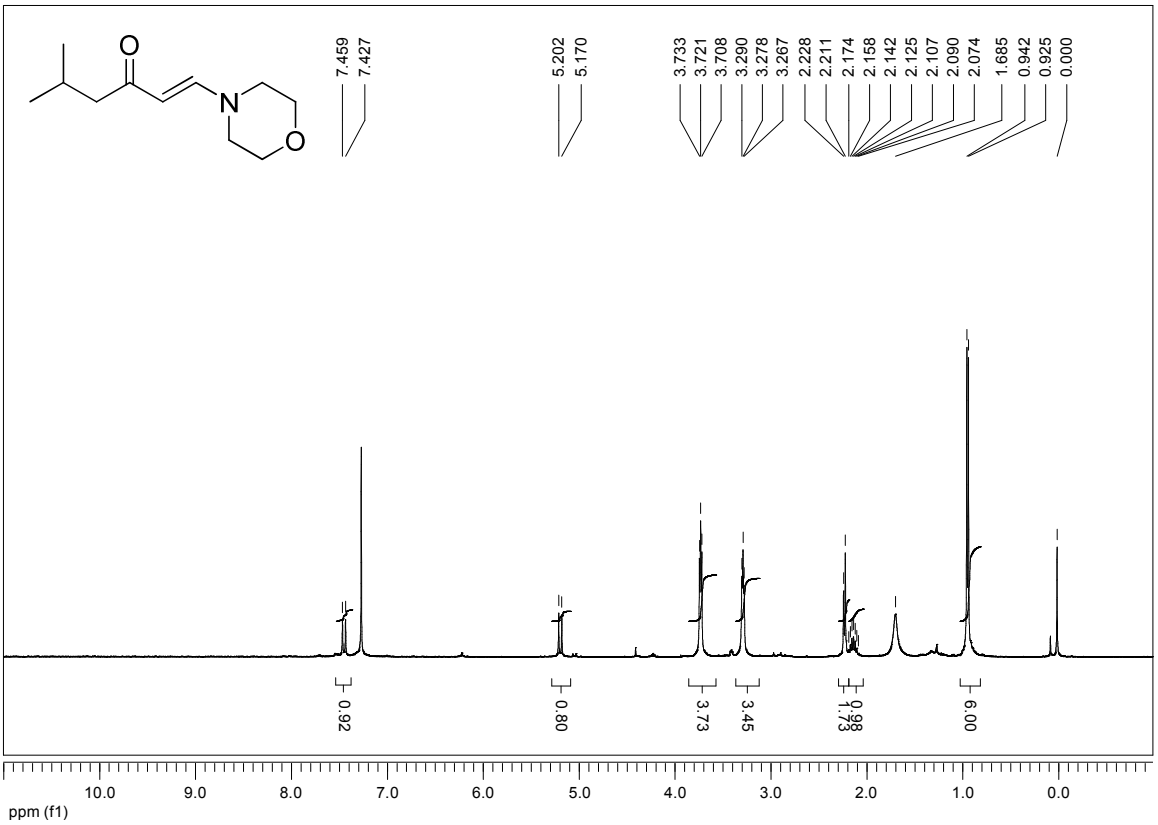
^{1}H NMR of **3h**



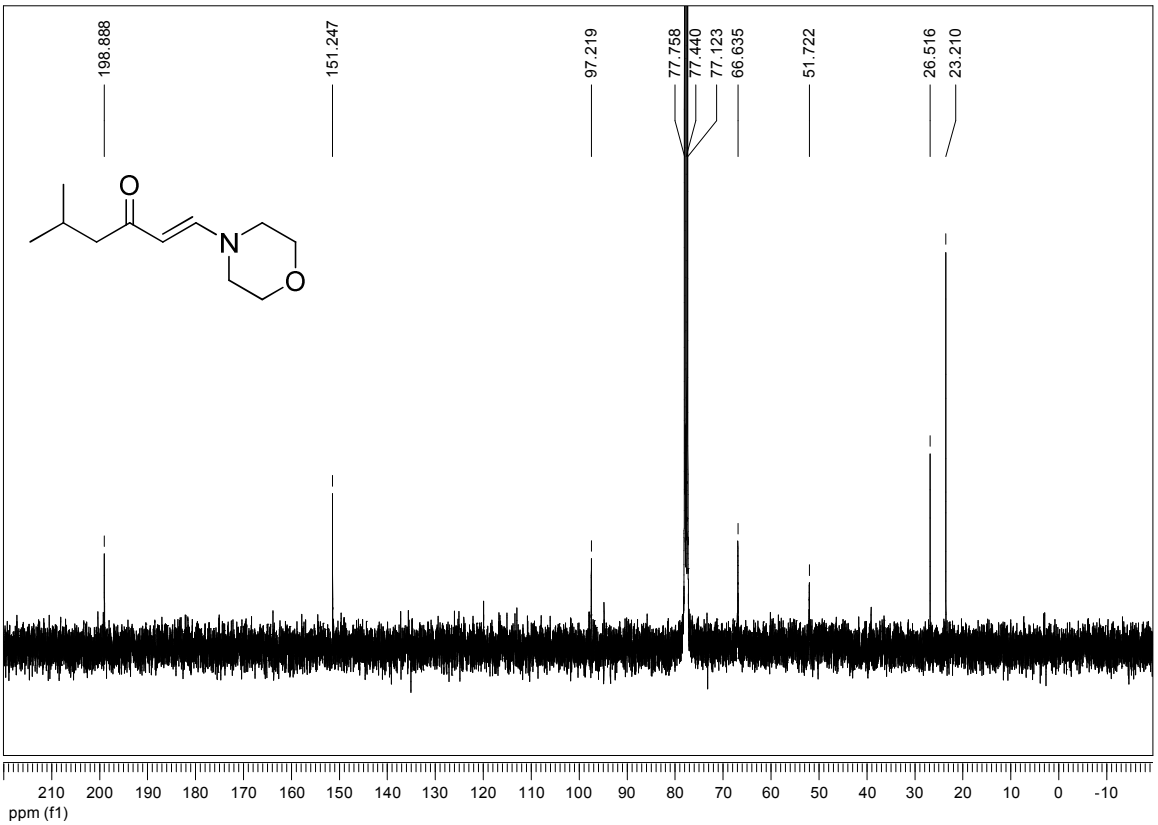
^{13}C NMR of **3h**



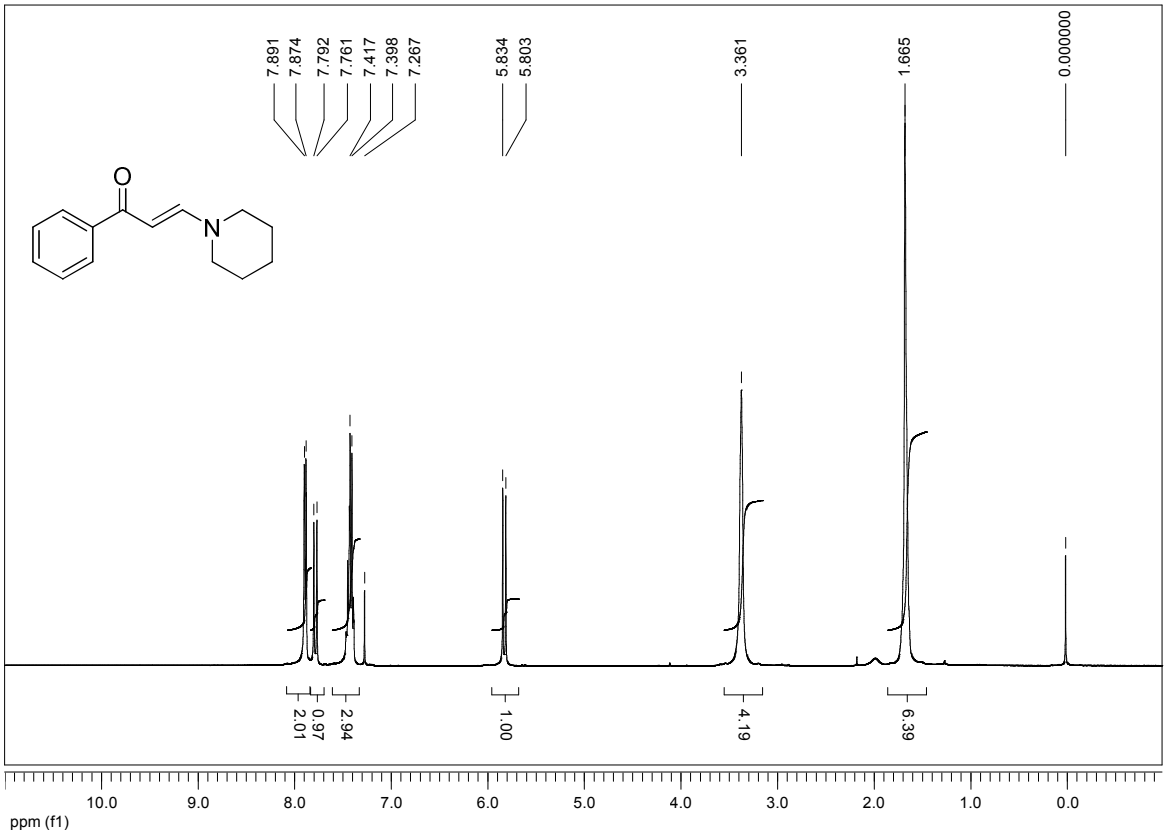
^{1}H NMR of **3i.**



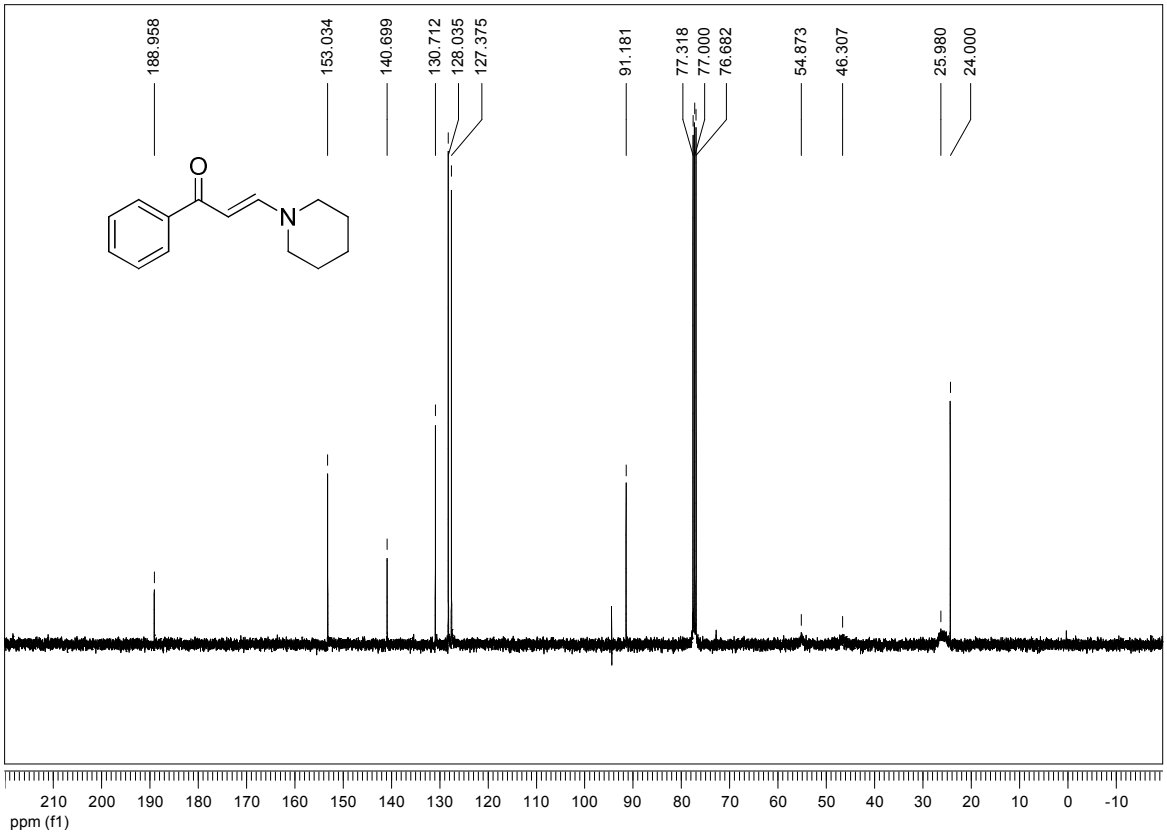
^{13}C NMR of **3i.**



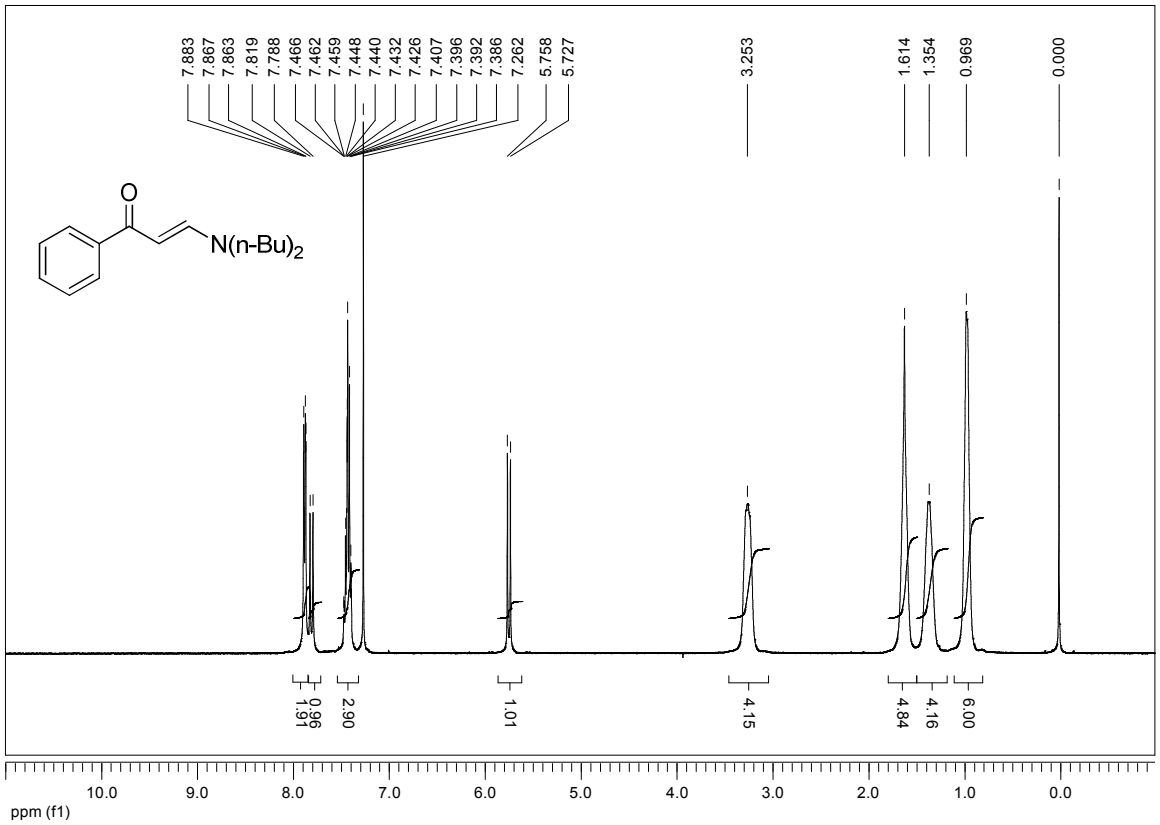
^{1}H NMR of **3j**



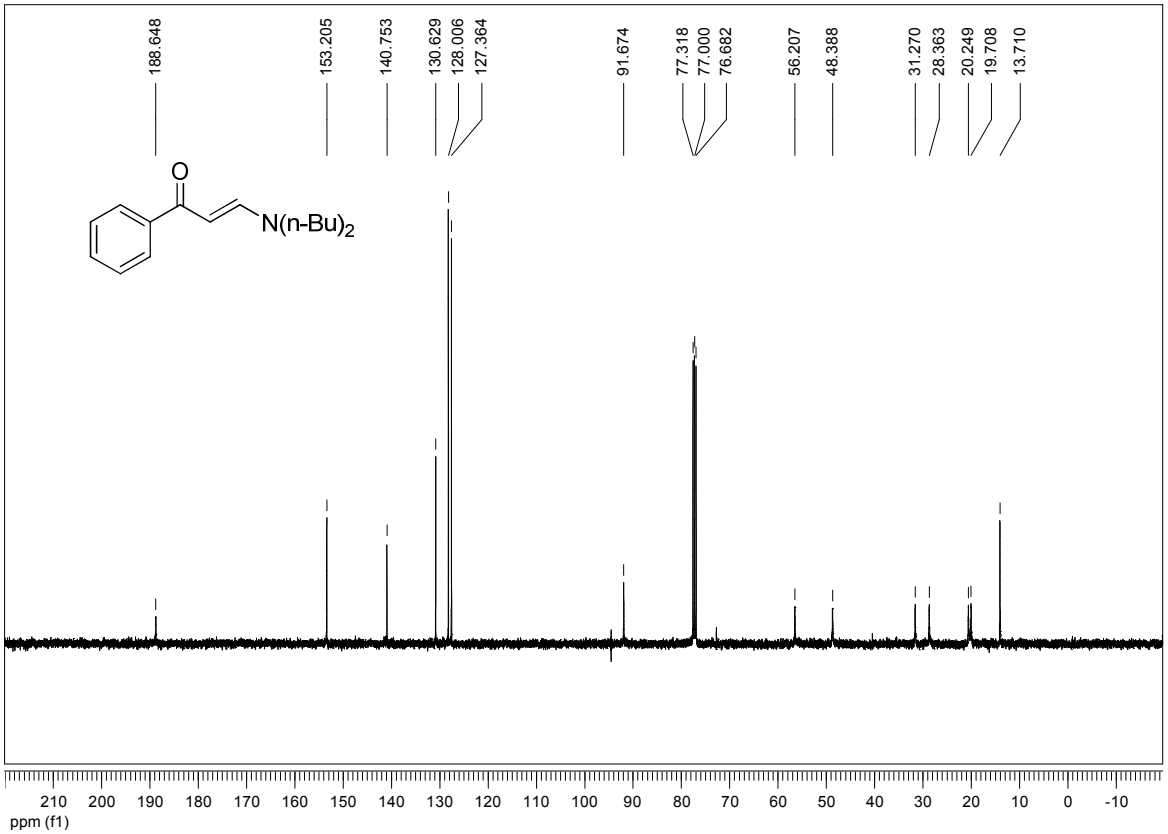
^{13}C NMR of **3j**



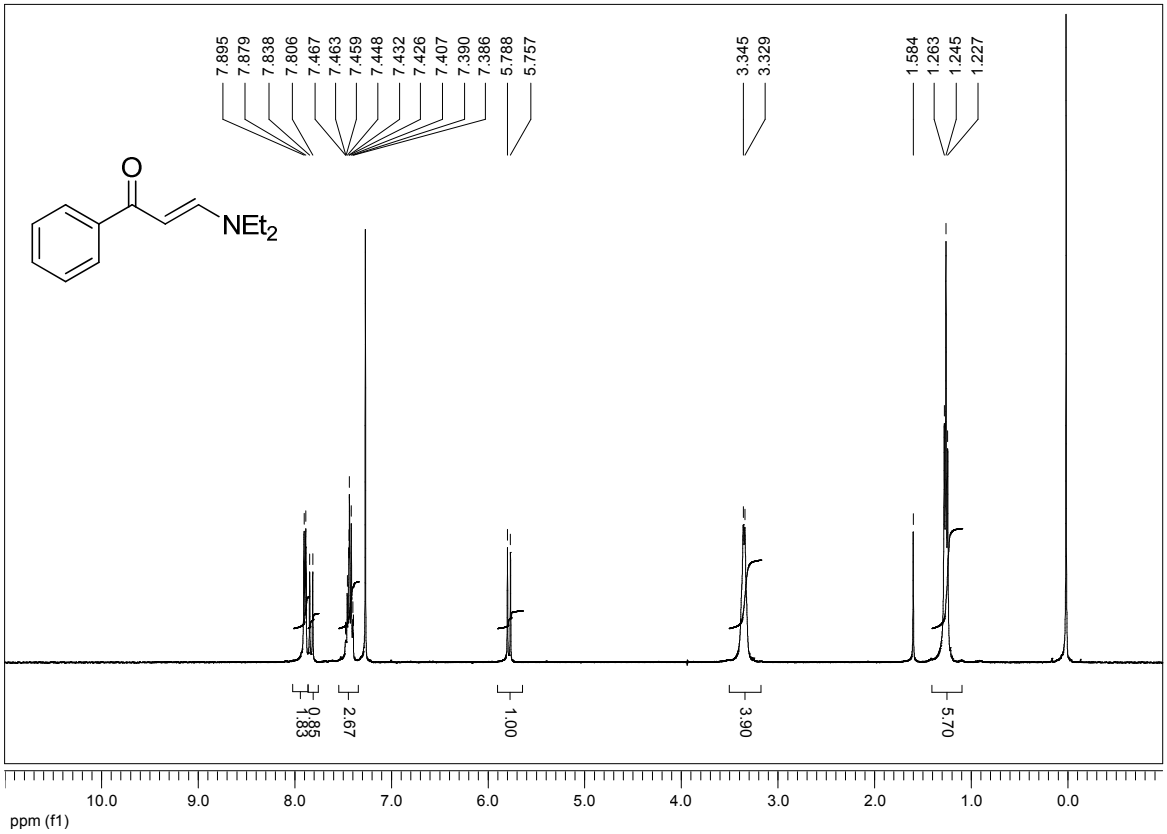
^{1}H NMR of **3k.**



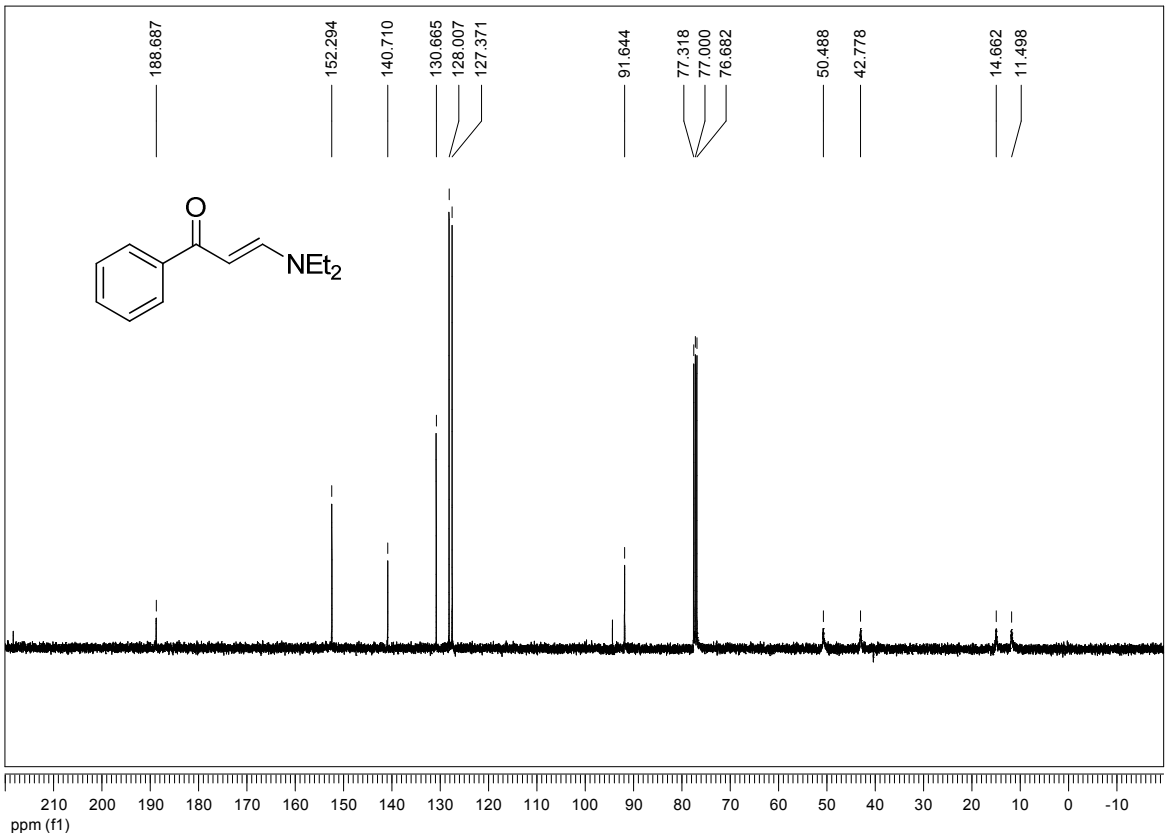
^{13}C NMR of **3k.**



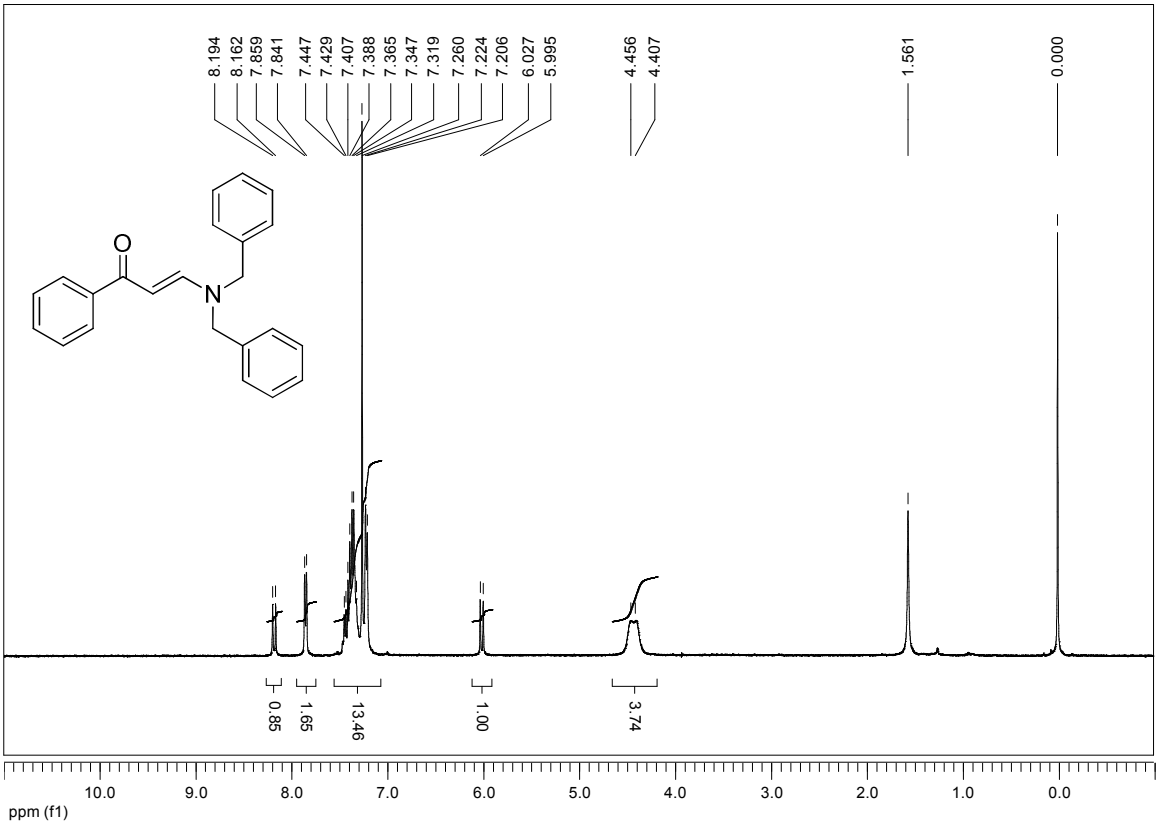
^{1}H NMR of **3l**



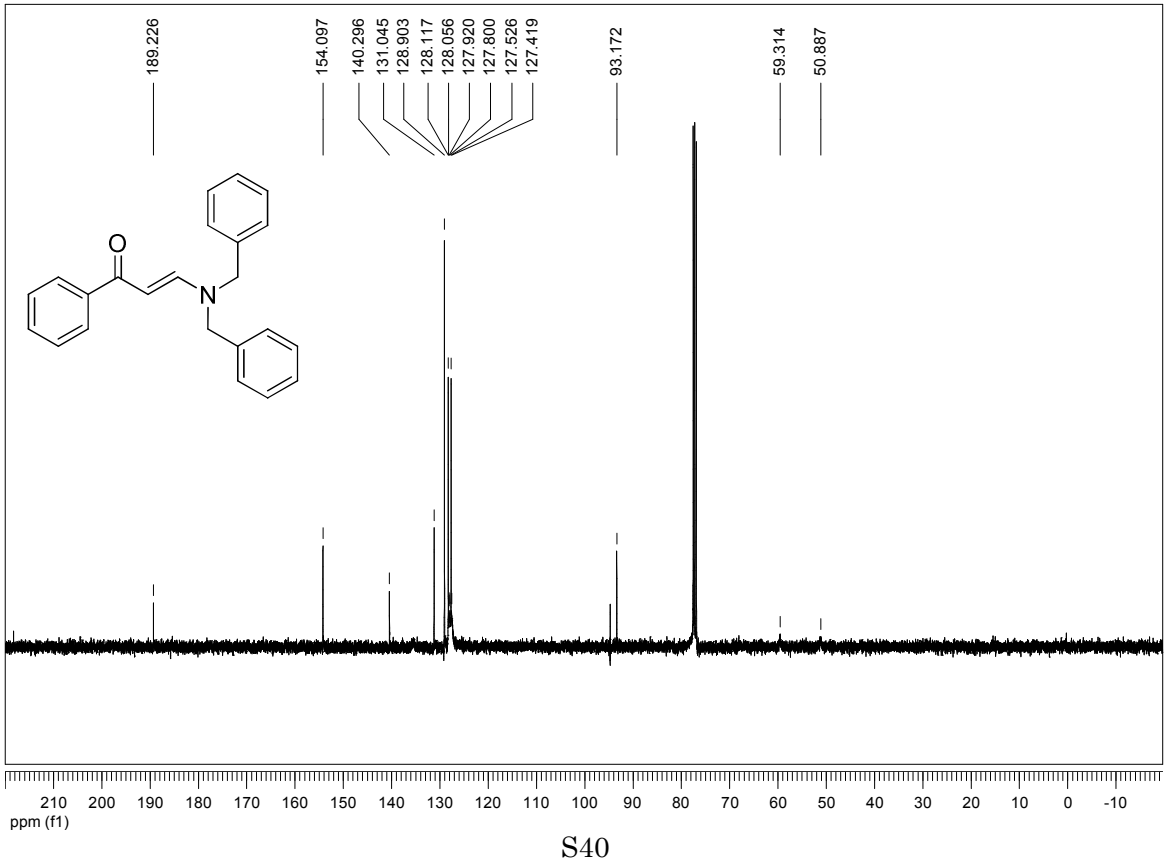
^{13}C NMR of **3l**



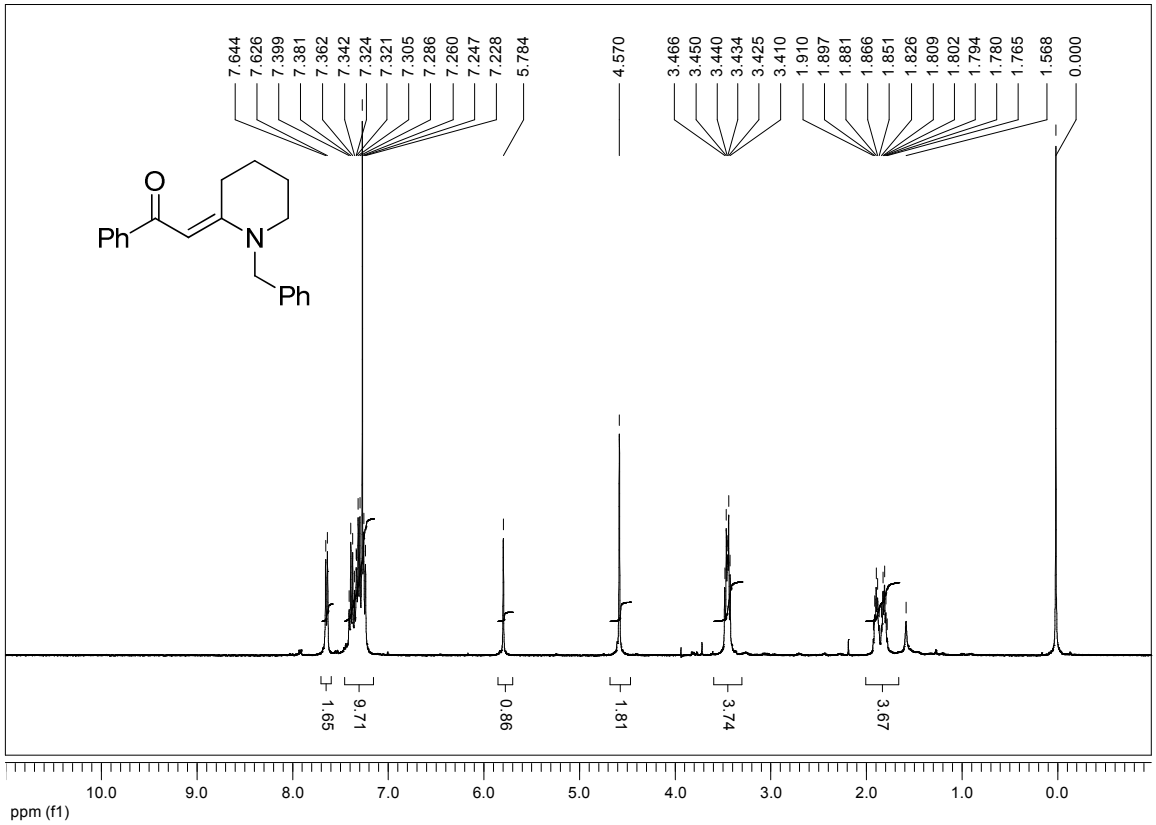
^{1}H NMR of **3m**



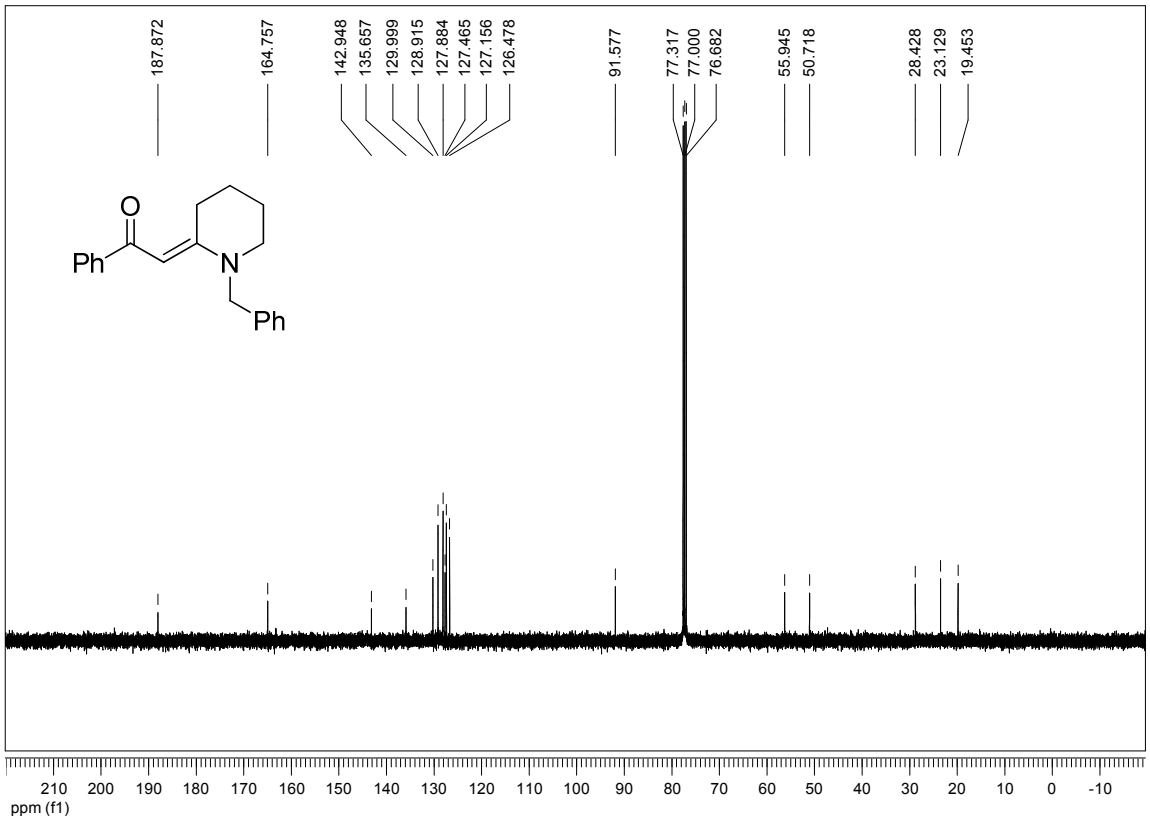
^{13}C NMR of **3m**



^{1}H NMR of **5**



^{13}C NMR of **5**



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